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INSIDE

Burn, Baby Burn!

ABSTRACT & COMMENTARY

Synopsis: *Being overweight is associated with symptoms of gastroesophageal reflux (GERD) in a dose-dependent way. This association is stronger for women than for men, particularly for premenopausal women and for those taking hormone replacement therapy (HRT). Weight loss reduces the risk of GERD.*

Source: Nilsson M, et al. *JAMA*. 2003;290:66-72.

THIS REPORT COMES FROM 2 POPULATION-BASED, CROSS-SECTIONAL case-control studies conducted in Norway. Data were collected from a total of 47,556 people in 2 separate surveys conducted about 10 years apart (1984-1986 for Helseunder-sokelsen I Nord-Trondelag 1 or HUNT 1, and 1995-1997 for HUNT 2). Written questionnaires distributed at health centers collected data on 813 variables. For this report, Nilsson and colleagues have focused on 58,596 individuals in the HUNT 2 survey who responded to a question about experiencing heartburn or regurgitation within the preceding 12 months. Because of the extensiveness of the questionnaire, Nilsson et al were able to control for every known relevant variable, and they used other "nonspecific gastrointestinal symptoms" (nausea, constipation, diarrhea) as control symptoms in the logistic regression model. After exclusion of pregnant women and those with incomplete data, 20,369 men and 22,994 women were included in the final analysis; 3113 (about 5%) reported severe heartburn and were considered "cases." The mean age of the group was 52 years and their mean body mass index (BMI) was 28.1 kg/m^2.

There was a moderate dose-dependent relationship between increasing BMI (above 25) and symptoms of GERD. This dose-dependent relationship was stronger in women than in men; the most obese men (BMI > 35) had about a 3.3-fold increased risk, but the most obese women had a 6.3-fold increased risk. This risk was less for postmenopausal women than premenopausal women (odds ratio, 4.2 vs 6.8). However, normal weight postmenopausal women who had ever taken estrogen-only HRT had more than twice the risk of GERD symptoms as did those normal-weight women who did not take reflux. The greatest risk of reflux symptoms was seen in women who had ever taken estrogen-only HRT and who had a BMI > 35;

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the likelihood of symptoms in these individuals was increased more than 33-fold compared with normal-weight people who had not taken HRT.

Nilsson et al also used data from the HUNT 1 study to assess the effect of weight change on the 72.8% of subjects who had participated in both studies. The risk of reflux was dose-dependently greater with increasing net BMI gain, controlling for all other variables. Further, a loss of more than 3.5 BMI units was associated with striking reduction in the risk of reflux symptoms.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

This is the first study to convincingly demonstrate a strong dose-dependent relationship between increasing weight and increasing symptoms of gastroesophageal reflux. Further, it documents reduced risk of symptoms with weight loss and increased risk with weight gain. There have been 3 prior population-based studies that addressed the relationship between obesity and GERD, including a previous one by the same authors.[1] They assert (and I agree) that in one of their previous studies,[2] they simply did not include enough obese people to show a relationship. The current epidemic of obesity is a relatively new thing. As we grow fatter, we will likely continue to discover new associations (none of them good) between being overweight and health outcomes. The other prior studies[1,3] did find a weak relationship between BMI and reflux but did not do separate analyses between men and women. They hypothesize that estrogen is a significant culprit in causing GERD symptoms and point out that obese women have greater synthesis of estrone in fatty tissue as well as greater circulating levels of unbound estradiol.

There are 2 bits of good news here: Weight loss appears to be associated with a reduced risk of GERD, and menopause without hormones may be associated with less heartburn. ■

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Is Sliding-Scale Insulin on the Slippery Slope?

ABSTRACT & COMMENTARY

Synopsis: *Adding sliding scale insulin to an inpatient's usual diabetic medications does not reduce rates of hyperglycemia or hypoglycemia or shorten length of stay.*

Source: Dickerson LM, et al. *Ann Fam Med*. 2003;1:29-35.

To ascertain the benefits of instituting a sliding-scale insulin (SSI) regimen of regular insulin in hospitalized patients, Dickerson and associates conducted a multicenter, randomized control study. They enrolled 153 adults with a comorbid diagnosis and a concurrent diagnosis of diabetes mellitus type 2 from 10 family practice residency programs. They excluded patients with diabetic ketoacidosis, hyperosmolar nonketotic state, hypoglycemia, pregnancy, acute myocardial infarction, hemodynamic instability, or acute cere-

brovascular accident and patients who could not take food or medicine orally. All patients continued their usual diabetic medications (oral drugs or intermediate-acting insulin alone or in combination with regular insulin). The study group received SSI in addition.

The study group (n = 75) and the control group (n = 78) were similar in age (62.5 vs 65.9 years), gender (37.3% female vs 32.1% male), race, and ethnicity. On admission they had similar blood glucose values (202.9 vs 186.4 mg/dL). They had similar comorbidities, which were primarily cardiovascular, pulmonary, infectious, and neurologic. Their usual diabetic medications were sulfonylureas, metformin, and thiazolidinediones. There were significantly more patients in the control group using intermediate-acting insulin (33.3 vs 50.0%).

All patients had fingerstick blood glucose determinations 4 times a day, and all were taking an American Diabetes Association diet. The study end points were blood sugars greater than 300 mg/dL (hyperglycemia) or less than 50 mg/dL (hypoglycemia), glycemic events (combined rates of hyper- and hypoglycemia), and length of hospitalization.

The addition of SSI resulted in no difference in any end point. The percentages of patients (study vs control) with hyperglycemia (33.3 vs 34.6%), hypoglycemia (8.0 vs 9.0%), and glycemic events (36.0 vs 35.9%) were not significantly different. In both groups the average number of glycemic events was 1.3. The length of hospitalization (5.0 vs 5.3 days) did not differ significantly.

On multivariate analysis 3 factors were associated with an increase in glycemic events: use of intermediate-acting insulin, blood glucose greater than 250 mg/dL on admission, and receipt of corticosteroids.

COMMENT BY ALLAN J. WILKE, MD

SSI regimens are passed down from senior resident to intern like family recipes. Like families arguing about who has the best recipe for spaghetti sauce, residents argue the virtues of the SSI they learned. In theory (at least according to my senior resident), use of SSI corrected for the alteration of glucose metabolism that comorbid disease wrought. SSI is not without problems. Patients are subject to an increase in needle sticks, and it ties up nursing time, a precious commodity these days. This is not the first article to call into question the use of SSI. Queale demonstrated a higher rate of hyperglycemia with SSI.[1] Gearhart reported shorter hospital stays when diabetes is treated proactively, rather than retroactively with SSI.[2] (Interestingly, the earliest reference I could find that argues against SSI was published in 1970,[3] early enough that my senior resident should have known better!)

Some cautions: This study examined only one SSI regimen. It was not aggressive in its regular insulin dosing (eg, 4 units for a blood glucose between 201 and 250 mg/dL), which is understandable since the SSI augmented rather than replaced usual therapy. It is possible that a more aggressive regimen may have produced different results.

Is there any reason to suspect that the patients in this study are different than the ones you treat? The demographics and comorbidities look very much like the adult patients in a general internal medicine or family practice to me. Although Dickerson et al do not discuss it, patients from residency practices tend to be poorer and more inclined to postpone admission until it is absolutely necessary. If that is the case here, then these patients may have been sicker than the ones you admit. If anything, that only strengthens the study's conclusions for me.

It is curious that patients using intermediate-acting insulin had more glycemic events and that patients in the control group were more likely to be using acting insulin, yet there was no difference between the 2 groups in rates of glycemic events.

Taking into considerations the limitations of this study (only diabetes type 2 patients who were not critically ill and who could take medicine orally), it is time to for SSI to join bloodletting and trepanation in the Museum of Medical Anachronisms. ■

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It's Time for West Nile Virus Again!

SPECIAL UPDATE

By Stan Deresinski, MD, FACP

West nile virus (WNV) was alien to North America before the summer of 1999. That year, WNV infection invaded New York City, establishing a beachhead that has now led to invasion of much of the United States, as well as intrusions into Mexico, Central America, and the Caribbean. WNV is clearly here to stay.

WNV was first detected in Uganda in 1937 with subsequent appearances in Asia, the Middle East, and East-

ern Europe. With the exception of a 1957 nursing home outbreak in Israel in which a number of those affected developed infections of the central nervous system (CNS), it generally produced sporadic mild febrile illness, with occasional outbreaks. This pattern changed after 1996 with the occurrence in Israel of outbreaks associated with more severe illness and frequent CNS involvement, a pattern followed by the US experience. This similarity of clinical illness is no surprise since the virus detected in 1999 in New York is virtually genetically identical to that isolated from a dead goose found in Israel in 1998.

While the numbers of cases of WNV infection in the United States were relatively small from 1999 through 2001, in 2002 an epidemiologic explosion occurred with 4156 cases, including 284 deaths, in 44 states plus the District of Columbia.[1]

WNV also demonstrated new methods of transmission and novel clinical syndromes. In addition to its usual mode of transmission by the bite of mosquitoes, WNV has been transmitted by percutaneous inoculation in laboratory accidents, by transfusion of blood products, via transplanted organs, via breast milk, and by the transplacental route.[2] The FDA hopes to introduce blood screening procedures this summer.

The most remarkable clinical findings have been the frequent occurrence of profound muscular weakness and of movement disorders. A syndrome closely resembling that of paralytic polio is, like that due to polio virus, the result of infection of anterior horn cells.[3] The observed movement disorders include tremors, myoclonus, and Parkinson's-like findings.

Diagnosis depends upon antibody tests and genome detection by polymerase chain reaction. Treatment remains supportive, although both ribavirin and interferon alpha are active against the virus in vitro. A therapeutic trial examining the safety of the latter agent received FDA approval in January of this year. This study, whose principal investigator is at New York Hospital in Queens, will enroll 40 patients with WNV encephalitis.

It is believed that yellow fever virus and its vector were introduced into the Americas in the 16th or 17th centuries as the result of the slave trade. The US Congress was driven from Philadelphia in the summer of 1793 by a yellow fever epidemic. Although eradicated from North America, yellow fever persists in tropical South America. Centuries later, another flavivirus, WNV, has found its way to the Americas and is in expansive mode, surprising us with some of its manifestations. It's time to get ready for the 2003 version of WNV infection in North America. At the same time, we should begin to look ahead—Could Japanese encephalitis virus, yet another flavivirus, make its way into North America? ■

Dr. Deresinski is Clinical Professor of Medicine, Stanford; Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center, Calif.

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New Hypertension Guidelines: JNC-7

ABSTRACT & COMMENTARY

Synopsis: *A new classification of blood pressure in adults is suggested, with normal blood pressure (BP) as < 120 mm Hg and < 80 mm Hg.*

Source: Chobanian AV, et al. *JAMA*. 2003;289: 2560-2571.

THE LONG-AWAITED JNC-7 REPORT WAS RECENTLY published in summary form; a more comprehensive manuscript will be forthcoming. JNC-7 takes into account many of the randomized controlled trials dealing with hypertension (HBP) published over the past few years, and thus, is very much up to date. Some highlights of the report are as follows:

1. A new classification of blood pressure in adults is suggested, with normal blood pressure (BP) as < 120 mm Hg and < 80 mm Hg. A new category, prehypertension, is defined as systolic pressure (SBP) 120-139 or diastolic (DBP) 80-89. In this category, pharmacologic treatment is indicated only if there is a "compelling indication," such as diabetes, vascular disease, or kidney disease. Stage 1 hypertension is now defined as SBP 140-159 or DBP 90-99, and stage 2 hypertension is SBP > 160 or DBP > 100. Drug treatment is mandated for both stages, with combination therapy more likely to be necessary in stage 2.

2. A thiazide-type diuretic is recommended as the first drug to be used except in patients with hyponaturemia or gout. Furthermore, a diuretic should be part of any multidrug combination.

3. The prevalence of hypertension is 50 million individuals in the United States. JNC-7 emphasizes the

marked prevalence of HBP in the elderly; data from the Framingham Heart Study suggests that individuals with a normal BP at age 50-60 have a 90% lifetime risk of developing HBP. Hypertension is the most common primary diagnosis in the United States, with only modest gains in awareness, treatment, and control of BP over the past 25 years. Recent data suggest that only one-third of the hypertensive population is under adequate control (NHANES survey).

4. Recent clinical trials indicate that antihypertensive treatment can reduce stroke incidence by 35-40%, acute myocardial infarction by 20-25%, and more than a 50% reduction in new onset heart failure.

5. There was an emphasis on how to accurately determine BP measurements in the outpatient setting, (2 measurements in subjects seated quietly for at least 5 minutes).

6. JNC-7 recommends self-measurement of BP at home to determine response to therapy, confirm adherence, etc. The goals of antihypertensive therapy are stated as "the reduction of cardiovascular and renal morbidity and mortality." JNC-7 emphasizes that the "primary focus should be on achieving the systolic BP goal." A generic target for BP of < 140/90 mm Hg is associated with decreased cardiovascular complications. In high-risk patients, such as those with diabetes or renal disease, the goal is < 130-80 mm Hg, which Framingham considers to be the optimal blood pressure.

7. Healthy lifestyles are strongly emphasized throughout the report, including weight control; adoption of the DASH diet, with increased intake of potassium and calcium rich foods, fruits and vegetables; moderation of alcohol consumption to < 2 drinks a day; and regular physical activity.

8. Pharmacologic therapy is simplified, with the admonition that a thiazide-type diuretic should be the basis of therapy, followed by any of the major classes of antihypertensive drugs. These include angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), beta blockers, and calcium channel blockers. Virtually no mention is made of outlier drugs for BP control in JNC-7 (eg, alpha blockers or CNS active drugs, such as clonidine). Chobanian and associates strongly emphasize that the majority of patients with HBP will require 2 or more medications to achieve goals. Furthermore, they recommend that drugs from different classes be used in polypharmacy. Therapy may be initiated with 2 drugs, particularly if baseline blood pressure is high and/or the subject is at increased vascular risk. Follow-up should occur monthly after initiation, and more frequently in stage 2 patients. When BP is at goal and stable, follow-up visits are recommended at 3-6 month intervals. Co-morbidities or high-risk conditions are emphasized, requiring specific choices of drug classes. These are quite obvious and include beta blockers for individuals with co-existing ischemic heart disease and an ACE inhibitor for those with heart failure, acute coronary syndromes, or postmyocardial infarction. Aldosterone antagonists are also recommended in heart failure. Heart failure patients with hypertension should have "fastidious BP and cholesterol control," with the mainstay of hypertensive therapy being an ACE inhibitor and beta blocker. ARBs and aldosterone blockers, along with loop diuretics, are also appropriate for late-stage heart failure. Diabetics should be routinely treated with 2 or more drugs, with an optimal blood pressure target. Physicians need to keep in mind that ACE inhibitors and ARBs favorably affect progression of diabetic renal disease.

9. A newly recognized high-risk group is individuals with chronic kidney disease, as manifest by creatinine of > 1.3 in women and > 1.5 in men or a GFR of < 60 mLs/m^2. Such individuals should be targeted for a BP < 130/80 mm Hg. Again, drugs acting on the renin angiotensin system (RAS) are suggested. Chobanian et al accept a modest rise in serum creatinine of up to one-third over baseline if and when an ACE or an ARB is used.

10. Emphasis is given to obesity and the metabolic syndrome, stressing the high-risk aspects of these increasingly common conditions. Hypertensive control in the elderly is also stressed. JNC-7 recommends starting with smaller drug doses in the elderly, watching for postural hypotension, while stressing control of systolic BP.

The conclusion of the report deals with how to best motivate patients with hypertension, stressing individual engagement in the process with a "patient-centered strategy and an estimation of the time needed to achieve the goal" established by the patient and the physician. Chobanian et al stress physician-stimulated motivation and empathy as influencing adherence to therapy. A final comment highlights population increases in consumption of saturated fat and salt and decreases in physical activity as being partly responsible for the epidemic of overweight and obesity, contributing to hypertension and related conditions.

■ COMMENT BY JONATHAN ABRAMS, MD

In the heels of many recent well-performed trials in hypertension, including ALLHAT, LIFE, HOPE, RENAAL, PROGRESS, UKPDS, ANBP2, as well the recent guidelines for treatment of hypertension in African-Americans and numerous algorithms and guide-

lines, there are few to no surprises in the official JNC-7 report. There has been considerable noise and confusion in the hypertension world for many years, particularly relating to the controversy over the safety of thiazide diuretics and the concern raised by some that calcium channel blockers may actually induce adverse events. The premature discontinuation of the alpha blocker arm in ALLHAT raised concerns that there may be unproven adverse effects of some classes of drugs. JNC-7 does not favor any single class of drugs, and even its recommendations for initiating therapy with a thiazide is not revolutionary. These drugs have been the cornerstone of hypertension guidelines for years, although they have fallen out of favor, in part to the aggressive marketing of the newer classes of agents, such as drugs that interfere with the RAS system and the calcium channel blockers. I view the most important aspects of this report to be as follows:

1. The emphasis on the concept that lower is better. Blood pressure control should be analogous to our approach to LDL cholesterol, with more aggressive targets for patients at the highest risk. Similar to the level of < 100 mg/dL for LDL cholesterol, the goal of < 120/80 in high-risk hypertensives makes sense and should be followed by all physicians who treat patients with HBP.

2. The emphasis that systolic BP is the most important target, in spite of previous teaching that treatment of diastolic hypertension is the gold standard. Most of the morbidity and mortality from cardiovascular disease, including stroke, is related to systolic hypertension, with a wide pulse pressure with only normal or mild elevations of diastolic pressure. Health care personnel must understand that a systolic BP of 150-160 mm Hg is not benign, but actually is a hazardous level requiring therapy.

3. Polypharmacy or multiple drug combinations should be the rule rather than the exception. It is important for physicians to initiate therapy with low doses of 2 different classes of drugs or be prepared to add a second and even a third drug class to achieve optimal control, rather than pushing the doses of drugs to high and potentially toxic levels. A diuretic should always be included with ACE inhibitor or ARB therapy. The focus on risk stratification is useful and is comparable to the NCEP ATPIII guidelines for lipids. Highest-risk patients are those with established vascular disease, diabetes, metabolic syndrome, or mild renal disease (proteinuria, elevated creatinine). The target BP in all of these conditions should be the "optimal" blood pressure of < 120/80 mm Hg. Hypertension may not be the sexiest subject for cardiologists and primary care physicians, but it is truly an important condition requiring commitment and vigilance. Highly effective drugs are available, which decrease events and save lives. JNC-7 is an effective road map for those who are not yet on board. ■

Dr. Abrams is Professor of Medicine, Division of Cardiology, University of New Mexico, Albuquerque, NM

Pharmacology Update

Influenza Virus Vaccine Live, Intranasal (FluMist)

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

THE FDA HAS APPROVED THE FIRST NASALLY ADMINISTERED flu vaccine. This cold-adapted, temperature sensitive, attenuated, trivalent vaccine is manufactured by MedImmune Vaccine, Inc. and marketed by MedImmune and Wyeth under the name "FluMist." The nasal flu vaccine should be available this fall.

Indication

The vaccine is indicated for active immunization for the prevention of infection caused by influenza A and B. It is indicated for healthy children and adolescents 5-17 years of age and healthy adults 18-49 years of age. It is not indicated for children younger than 5 years of age or adults 50 years of age or older.[1]

Dosage

The recommended dose for children and adults aged 9-49 years is a single dose (0.5 mL) administered prior to exposure to influenza. For children 5-8 years, 2 doses are administered about 60 days apart (46-74 days). Approximately one-half of the dose (0.25 mL) is administered into each nostril.[1] The 2003-2004 vaccine will contain A/New Caledonia/20/99 (H1N1), A/Panama/2007/99(H3N2) (A/Moscow/10/99-like), and B/Hong Kong/330/2001.[1] The vaccine may be thawed in a refrigerator prior to administration but for no more than 24 hours.

Potential Advantages

The intranasal vaccine provides an alternative to the inactivated, parenterally administered vaccine.

Potential Disadvantages

The intranasal vaccine is not indicated in the very

young (< 5 years of age) and the old (> 49 years of age). Two doses are required for children (5-8 years of age). In a large safety study, children < 5 years of age who received the nasal vaccine were found to have an increased rate of asthma and wheezing within 42 hours of vaccine administration.[2] The vaccine should not be administered to individuals with chronic underlying medical conditions that may predispose them to severe influenza infection.[3]

Adverse events seen with intranasal flu vaccine were nasal congestion (7-11%) and fever (4%) in children, and score throat (10-15%) in adults.[3] The vaccine requires storage in a non-frost-free freezer that maintains temperature of -15°C or less.

Comments

The first intranasal flu vaccine is a cold-adapted, temperature-sensitive, live attenuated vaccine. The cold-adaptive and temperature-sensitive process results in strains that replicate best at 25°C and are restricted in replication at 37°C. The phenotypes do not produce classic influenza viruses in animal models of human infections.[1] Once administered, the attenuated viruses replicate in the nasopharynx and produce protective immunity. In 2 placebo-controlled trials in children (60-84 months of age) (n = 782), the vaccine had efficacy of about 87% based on cultured-confirmed influenza.[1] The point estimates and 95% confidence interval were 87.4% (59.4%-97.9%) in one and 86.9% (70.8%-94.1%) in the other. In the Adult Effectiveness Study (n = 3637), the primary end point was reduction in the proportion of participants with one or more episodes of any febrile illness or, more specifically, severe febrile illness or febrile upper respiratory illness.[1] No reduction in any febrile illness was observed, but a 19.5% (95% CI, 3-33.2%) reduction in severe febrile illness and a 23.7% (95% CI, 6.7-37.5%) reduction in febrile upper respiratory illness was noted.[1] The intranasal vaccine was compared to an inactivated vaccine and placebo in a challenge study in 92 healthy adults. These volunteers were randomized to the 3 arms and then challenged with a previously susceptible wild-type influenza virus. Protective efficacy (based on laboratory-documented influenza) was 85% for the intranasal vaccine and 71% for the inactivated vaccine (not statistically different). Eighty percent of vaccine recipients shed at least one vaccine strain with a mean duration of 7.6 days. The public health significance is not clear. The probability of acquired transmitted virus is unlikely.[1] The vaccine is generally well tolerated. The cost of the intranasal vaccine is $46 per dose. The cost of the inactivated influenza vaccine for the last season (02-03) was about $7 per dose.

Clinical Implications

The introduction of an intranasal influenza vaccine offers an alternative to the parenteral influenza vaccine, although at a much higher cost. It use is limited to use in the generally healthy population ages 5-49.

The vaccine is not indicated for those at highest risk, children younger than 5 years of age and adults older than 65 years of age. ■

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CME Question

3. Which of the following are all associated with an increased risk of symptoms of gastroesophageal reflux?

a. Obesity, weight gain, premenopausal state, hormone replacement therapy
b. Obesity, weight gain, premenopausal state, male gender
c. Obesity, weight gain, postmenopausal state, hormone replacement therapy
d. Obesity, weight loss, premenopausal state, hormone replacement therapy
e. Alcohol abstinence, weight gain, premenopausal state, hormone replacement therapy

4. When added to a patient's usual diabetic medications, sliding scale insulin is associated with:

a. less hypoglycemia.
b. less hyperglycemia.
c. more injections.
d. shorter hospital stays.

5. The most important new recommendation in JNC-7 is:

a. hypertension is a risk factor for CAD.
b. hypertension needs to be better controlled.
c. to lower target blood pressures.
d. diuretics are important agents.

Answers: 3 (a); 4 (c) 5 (c)

Correction

CME question #28 in the June 29 issue should have appeared in the July 15 issue. The corresponding article concerning warfarin dosing appears on page 99. We regret any confusion this might have caused. ■

By Louis Kuritzky, MD

Prognostic Value of Ambulatory Blood-Pressure Recordings in Patients with Treated Hypertension

AMBULATORY BLOOD PRESSURE monitoring (ABPM) has been available for more than a decade, yet it has not attracted routine application in clinical practice. Several factors have recently stimulated increased interest in ABPM, not the least of which is the acknowledged association between increased ABPM and adverse clinical outcomes. Indeed, ABPM measurements have been shown to correlate better with presence of target organ damage than office blood pressure measurement. Recently, Medicare has expanded coverage to include payment for ABPM when performed for suspected white-coat hypertension.

Clement and colleagues prospectively studied hypertensive subjects (n = 157) who were followed using both ABPM and office BP measurement for a mean of 5 years. They measured relative risk of subsequent cardiovascular events by increments in ABPM 24-hour mean BP, systolic BP, diastolic BP, and nocturnal BP, adjusted for gender, smoking, diabetes, cholesterol, BMI, and office BP.

For each 1 standard deviation increase in ABPM, the relative risk of cardiovascular events increased 34% for 24-hour mean BP, 30% for mean ABPM systolic BP, and 27% for mean ABPM diastolic BP. Although the prognostic information obtained from ABPM was consistent and provided information beyond that obtained with simple office BP, it did not predict all-cause death. As ABPM becomes more accessible, less costly, and more often covered by third-party payers, it may find an increasing role in standard care. ■

Clement DL, et al. N Engl J Med. 2003;348(24):2407-2415.

Tazarotene Cream in the Treatment of Psoriasis

TAZAROTENE (TZT) IS A RECEPTOR-selective retinoid used topically. Tazarotenic acid, the primary metabolite of TZT, binds to the retinoic acid receptor-gamma sites in the keratinocyte nucleus. Effects of TZT upon gene transcription include normalization of abnormal keratinocyte differentiation, reduction of inflammation, and reduction of epidermal hyperproliferation, each of which plays an important role in cutaneous psoriasis (PSR). Although TZT gel formulations have already been demonstrated to be effective in PSR, local adverse effects have been problematic. The cream formulation of TZT was developed in an attempt to reduce these adversities. The study included 1303 patients with PSR who applied TZT cream (or vehicle) once daily for 12 weeks.

Clinical success was achieved with TZT cream and persisted through a post-treatment observation period (12 weeks). Weinstein and colleagues mention that local adverse effects were seen with the cream such as pruritus, burning, erythema, and stinging, but no statistical comparison between adverse effects seen with the cream formulation vs earlier studies using the gel formulation were provided. Nonetheless, Weinstein et al comment that availability of both gel and cream formulation will offer clinicians a greater diversity of therapeutic choices for psoriasis. ■

Weinstein GD, et al. J Am Acad Dermatol. 2003;48:760-767.

Antihyperglycemic Effect of Oolong Tea in Type 2 Diabetes

ANIMAL STUDIES HAVE SHOWN THAT tea consumption can reduce plasma glucose. Teas fall into 3 primary categories: green, oolong, and black, which, though they all come from the same plant species, are differentiated by the fermentation technique with which they are processed. Green tea is not fermented, oolong is partially fermented, and black tea is fully fermented.

Study subjects were 20 Taiwanese diabetic men and women randomly assigned (cross-over design) to 4-week sessions of drinking either water or oolong tea. Daily consumption of oolong tea was 50 ounces, with specific instructions for ensuring consistency of brewing methodology. The patients in this study were already receiving oral hypoglycemic agents.

Oolong tea reduced plasma glucose to a statistically significant and clinically relevant degree: 220 mg/dL (pretreatment) to 162 mg/dL (post-treatment). Water had no significant effect upon glucose levels. There were no adverse effects attributable to Oolong tea, although the strength of the tea brewed was acknowledged to be greater than that consumed in the typical Taiwanese diet. This study supports the role of oolong tea to enhance glucose control in type 2 diabetes. ■

Hosoda K, et al. Diabetes Care. 2003;26(6):1714-1718.

In Future Issues: The Outpatient Bleeding Risk Index