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INSIDE

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What's the Frequency, BP?

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

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Dr. Wilke reports no financial relationships relevant to this field of study.

Synopsis: *A strategy of annual screening of blood pressure was as sensitive and more specific than the usual practice of measuring it at every office visit.*

Source: Garrison GM, Oberhelman S. Screening for hypertension annually compared with current practice. *Ann Fam Med* 2013;11:116-121.

THIS RETROSPECTIVE, CASE-CONTROL STUDY LOOKED AT FAMILY MEDICINE patients from the Mayo Clinic in Rochester, MN, to determine whether measuring blood pressure (BP) annually is more specific and just as sensitive as measuring it at every visit. Patients were 18-75 years old, did not carry the diagnosis of hypertension (HTN), and had been active in the practice from 2005-10. They excluded patients with diabetes mellitus, coronary artery disease, and chronic kidney disease and who were pregnant or were taking antihypertensive medications for something other than HTN (e.g., migraine prophylaxis, peripheral edema).

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Using International Classification of Diseases (ICD-9) billing code 401.x, they randomly selected 236 patients who were diagnosed with HTN (defined as a systolic BP [SBP] ≥ 140 or a diastolic BP [DBP] ≥ 90, average of at least two readings on at least two visits) during the study period and 500 who were not. Many patients were excluded from the study for either having only one elevated BP measurement, never having a diagnosis of HTN, or being diagnosed with HTN before the start of the study, but not having an ICD-9 401.x billing code. The final pools had 68 patients who were diagnosed with HTN during the study period and 372 who weren't. The patients were similar in gender, smoking status, and number of visits per year, and differed in age, body mass index (BMI), and, not surprisingly, average BP. HTN patients were older (47.6 vs 41.2 years old), more obese (BMI 33.6 vs 28.6), and had higher SBP (135.3 vs 114.7) and DBP (82.7 vs 70.1). The two groups had 2.5 and 1.9 visits per year, respectively.

The authors compared two screening strategies. The first strategy ("usual") measured BP at every visit. The second strategy ("annual") was simulated. If the patient was being seen for a health maintenance visit, that BP was used. If no, and if the last BP was measured more than a year earlier, then that BP was used. The usual strategy identified all 68 HTN patients. It also identified 110 patients in the no-HTN group who had at least one BP ≥ 140/90. This yields a sensitivity of 100% (68/68, 95% confidence interval [CI], 92.2%-100%) and specificity of 70% (262/372, 95% CI, 65.2-75.0%). The annual strategy identified 63 HTN patients (sensitivity 93% [63/68], 95% CI, 83.7-97.6%), and 67 no-HTN patients with at least one BP ≥ 140/90 (specificity 82% [305/372], 95% CI, 77.7-85.8%). The sensitivities were not significantly different statistically, because the 95% CIs overlapped. The difference in specificities did reach statistical significance.

■ COMMENTARY

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) recommends a screening interval of every 2 years for people who have BP < 120/80 and annually for people who are prehypertensive (SBP 120-139 or DBP 80-89).

The authors argue that the patients who were missed by the annual strategy would have eventually been diagnosed, and since end-organ damage from HTN occurs slowly, even delayed treatment would mitigate it. They also argue that the lower false-positive rate with annual screening (18% [67/372] vs 30% [110/372]) results in fewer patients undergoing a work up for HTN.

Measuring BP in the office is not the most accurate way of screening for HTN, and it may not be the most cost-effective.[1] A meta-analysis published in 2011 compared ambulatory blood pressure monitoring (ABPM), the gold standard, to office and home monitoring, and found both to be lacking in sensitivity and specificity and recommended ABPM for individuals near the diagnostic cutoff, before subjecting them to lifelong medication management and its adverse effects.[2] Retrospective, case-control studies at a single site are not the pinnacle of evidence-based medicine. I would not recommend that you change your modus operandi of screening for HTN based solely on this article. The best that can be said is that it generates questions that should be answered in double-blind, randomized, controlled studies. So why review this article? Three reasons. First, HTN is a factor in two of the top five causes of death (heart disease and stroke) in the United States in 2011[3] and treating HTN reduces mortality.[4,5] Second, we desperately need to learn to work smarter, not harder. If, as a result of the Affordable Care Act, we are going to care for a much larger group of people in this country, many of whom are hypertensive, we have to change the way we do it. If this study is correct, we can shave valuable minutes off our visits by not measuring BP at every visit in a low-risk population (no diabetes, no heart disease, no kidney disease, no pregnancy). Finally, avoiding unnecessary work up (and expense) of false-positive diagnoses is vital if we are to make the best use of our limited resources.

We have all been waiting for publication of JNC-8. It was promised by the end of 2012.[6] Keep your ear to the ground — word is that the diagnostic and treatment algorithms will be simpler than JNC-7. ■

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Questions & Comments
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Exercise Benefits Patients with Parkinson's Disease

ABSTRACT & COMMENTARY

By Jeffrey Gross, MD

Clinical Associate Professor of Rehabilitation Medicine, NYU School of Medicine, Adjunct Clinical Assistant Professor of Rehabilitation Medicine, Weill Cornell Medical College

Dr. Gross reports no financial relationships relevant to this field of study. The article originally appeared in the May 2013 issue of Neurology Alert.

Synopsis: *Exercise, both aerobic as well as stretching and strengthening, improves motor function and gait in patients with Parkinson's disease.*

Source: Shulman LM, et al. Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease. *JAMA Neurol* 2013;70:183-190.

There is growing interest in the use of exercise training to improve mobility and function in patients with early Parkinson's disease (PD). A recent literature review showed that there were 75 clinical trials of physical training for PD.[1] The results of these trials have been promising. However, the majority of the studies were limited by methodological flaws.

Shulman et al performed a prospective, randomized, single-blind, parallel-group clinical trial of efficacy of three types of physical exercise for PD: 1) higher-intensity treadmill (HITM), 2) lower-intensity treadmill (LITM), and 3) stretching and resistance (SR). The primary objective of this clinical trial was to compare the efficacy of these three types of physical exercise to improve gait, fitness, and strength in patients with PD. The additional objectives were to study the efficacy of exercise to reduce disability and nonmotor symptoms in PD. The criteria for eligibility included a diagnosis of PD with no atypical signs or exposure to dopamine-blocking drugs, a Hoehn and Yahr stage of 1 to 3, the presence of mild-to-moderate gait or balance impairment, an age of 40 years or older, and no significant dementia. Exclusion criteria were unstable medical or psychiatric comorbidities, orthopedic conditions restricting exercise, or active participation in a regular exercise program before enrollment.

A screening treadmill exercise test was used to determine cardiopulmonary safety and neuromotor capacity to participate. The total duration of the study was 4 months. Initial evaluations included medical history and physical and neurologic examinations. Baseline and post-training assessments were performed by physicians and staff blinded to participants' treatment group. All evaluations were undertaken while the participants were in the "on" periods from medications, or within 3 hours of medication dosing.

Pre- and post-training maximum oxygen ventilation (VO_2 max) was assessed during treadmill exercise with the endpoint being voluntary exhaustion. Gait assessments were performed before and after training. The 6-minute walk (6MW) was the primary motor outcome measure. Participants were instructed to cover as much distance as possible in 6 minutes, turning every 30 meters. Other gait measures were two 10-meter walks (self-selected and fastest comfortable pace) and a 15-meter fast gait. Muscle strength was assessed with a 1-repetition maximum strength test performed before and after training in all study groups for leg press and leg extension. Strength in each leg was tested separately on isotonic weight machines. Disability and physical activity assessments were tabulated. Nonmotor symptom assessments also were performed before and after training.

Sixty-seven participants in the study were randomized into three groups that trained three times per week for 3 months under the direct supervision of exercise physiologists. Vital signs were monitored. All participants wore a non-weightbearing harness to eliminate the risk of falls. The HITM group exercised up to 30 minutes at a speed and incline that eventually resulted in a heart rate of 70-80% of their maximum (220 minus age). The LITM group walked at a comfortable pace for up to 50 minutes. The incline and speed remained constant. Their heart rate remained in the range of 40-50% of their calculated maximum. The SR group did two sets of 10 reps on leg extension, leg press, and leg curl machines. Weight was increased as tolerated. Stretching was performed as well.

There were no serious adverse events during the study. The results revealed improvements in all three groups for the 6MW. The greatest gains were made by the LITM group (12%), followed by the SR (9%) and the HITM (6%) groups, but the differences were not statistically significant between groups. The LITM group also made significant gains in the other gait measurements. VO_2 max increased in only the HITM and LITM groups. Lower extremity muscle strength only increased in the SR group. No significant changes were noted in disease severity, disability, or nonmotor symptoms in any of the groups.

■ **COMMENTARY**

The above results confirm the value of a regular exercise program for PD patients in the early stage of disease. Low-intensity treadmill exercise was proven to be safe, well tolerated, and beneficial in improving function and cardiovascular fitness. Resistance exercise leads to increased strength, as would be expected. A combination of these interventions seems warranted in all early PD patients who are medically well and able to participate. Although the exercise programs did not result in improvements in disability or quality of life, these variables did not deteriorate during the study either. This reflects the study's main limitation — there was no non-exercise control group. ■

Reference

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Is Your Smart Phone Spreading Infection?

ABSTRACT & COMMENTARY

By David J. Pierson, MD

Professor Emeritus, Pulmonary and Critical Care Medicine, University of Washington, Seattle

Dr. Pierson reports no financial relationships relevant to this field of study. The article originally appeared in the May 2013 issue of Critical Care Alert.

Synopsis: *Bacteria were present on the cell phones of all hospital clinicians studied, with potentially pathogenic microorganisms isolated from 29% of them. Contamination with pathogens was found more commonly with smart phones than with non-smart phones, and by multivariable analysis no other factor was associated with this difference.*

Source: Lee YJ, et al. Contamination rates between smart cell phones and non-smart cell phones of healthcare workers. *J Hosp Med* 2013;8:144-147.

Lee and colleagues administered questionnaires and performed bacterial cultures on the cellular phones of 203 clinicians (39% physicians, 52% nurses, 9% medical assistants) working in three university-affiliated teaching hospitals in Seoul. The questionnaire included data on participant demographics (age, gender, occupation) as well as behavior regarding cell phone use (type of cell phone, frequency and reasons for use, and cleaning of cell phones). The investigators touched the anterior and posterior surfaces of the phones onto blood agar plates and classified the recovered bacteria according to pathologic potential. Among probable pathogenic microorganisms, representative drug-resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus*, and imipenem-resistant *Acinetobacter baumannii* were categorized as drug-resistant pathogens. The participants' mean age was 29 years and 79% were women. A total of 115 (57%) were smart phone users and 88 (43%) used non-smart phones. The smart phone users were slightly younger (28 vs 29 years, $P = 0.03$), but this was the only significant difference between the groups. Only a minority of all cell phone users reported taking special measures to clean them.

All 203 cell phones had positive cultures: 4% had a single organism recovered, 19% had two organisms, and 76% had three or more. The most commonly cultured microorganism was coagulase-negative staphylococci, isolated from 96% of the phones. Gram-positive bacilli and *Micrococcus* species were also frequently recovered. Probable pathogenic bacteria were isolated from 58 cell phones (29%). *S. aureus* was the most common of these, and it was MRSA in 8 of the 50 instances. *Acinetobacter baumannii* was recovered from five phones. Probable pathogens were isolated more often from smart phones (35% vs 20% of non-smart phones, $P = 0.03$). The total colony count of probable pathogens from smart phones was also higher (average, 5.5 vs 5.0 from non-smart phones, $P = 0.01$). Among all the factors examined for possible association with phone contamination, only the phone's being a smart phone was found to be a risk factor for contamination by bacteria with pathogenic potential (adjusted odds ratio [OR] 4.02; 95% confidence interval [CI], 1.43-11.31; $P = 0.01$). Using the cell phone more than 10 times during working hours appeared to be associated with pathogen contamination; however, this correlation failed to reach statistical significance (OR, 2.9; 95% CI, 0.9-9.3; $P = 0.07$).

■ **COMMENTARY**

This study found that health care workers' smart

phones were more frequently contaminated with potentially pathogenic bacteria than non-smart phones. The authors postulate two reasons for this — that smart phones have larger surfaces that are more often touched by the user's fingers, and that they may be used more times during the day, since clinicians can use them for more work-related tasks than non-smart phones.

Other studies have documented frequent bacterial contamination of the cell phones of health care workers — along with their stethoscopes and various parts of their attire — as well as of the bed rails, monitors, bedside curtains, computer keypads, and other features of the patient's immediate environment. Direct linkage between such contamination and specific cases of hospital-acquired infection has generally been lacking, although it is hard to ignore the possibility of this or measures aimed at avoiding it. Cell phones are now carried by virtually all health care workers. Today, more and more of these are smart phones, which are increasingly being integrated into clinical and administrative aspects of critical care. How concerned we should be about their contamination with potential pathogens is not entirely certain, but we should be aware of the fact that such organisms are present not only on our hands but also on the things we carry around with us. ■

Brief Report

Bedbug Detection Squad

By Carol A. Kemper, MD, FACP

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Dr. Kemper does research for Abbott Laboratories and Merck. *The article originally appeared in the May 2013 issue of* Infectious Disease Alert.

Source: Vaidyanathan R, Feldlaufer MF. Bed bug detection: Current technologies and future directions. *Am J Trop Med Hyg* 2013;88:619-625.

Remember that scene in Doc Martin when he travels to London for a conference, and while his lady awaits his affection in a tiny negligee, he methodically strips the bed looking for bed bugs? How many of us make that a habit now when traveling?

Detection and control of bedbugs has become a busy industry the past decade, as estimates suggest 100-fold increase in the bed bug population. Bed bug bites vary from a few annoying bites to dramatic infestations, sometimes resulting in severe allergic reactions, delayed hypersensitivity reactions, and even anemia. I've seen patients come in with hundreds of bites, desperate for information and relief.

There are a number of methods and technologies to detect (and possibly control) bed bug infestations, including newer technologies pending patent. Visual inspection of beds and furniture for bugs, exuviae, and fecal droplets is cheap and easy — but you have to know what you're looking for and accuracy drops off with lesser infestations. It is also time-consuming (having to remake all those beds). There are a number of passive methods used, most of which employee glue or adhesive "traps," which vary in price from a few cents to $30 for a 12-pack. These are undoubtedly better than passive inspection, especially if you are staying in a place for more than one night. But the traps must be manually removed and inspected, and they often have a mix of live and dead bugs stuck to them — and the traps are not specific for bedbugs so can attract other insects (some people might object to this). Another passive method is a coaster trap for furniture and bed legs, which can be left for a week at a time, and reportedly trap 6-7 times the bed bugs of other passive traps. But they too need to be removed and inspected, and are also non-specific for bed bugs. They cost anywhere from $34 to $80 for a 12-pack.

Active traps can employ a number of methods, including heat and CO_2, which are the two most effective attractants, bringing in bugs at night wanting to feed. Traps based on CO_2 productions are, however, more costly, varying in price from $400 to $999, and require refillable CO_2 cartridges. In addition to cost, these systems also require visual inspection and removal of traps with live bugs and their feces, and operators often complain about the bulky cartridges, mechanical problems with the dispersal systems, and the constant hissing sound of the CO_2 being dispersed. One study found that a homemade passive trap using dry ice was more successful than more expensive commercial traps using CO_2 — the homemade dry ice system caught as many bugs in one day as the more expensive traps caught in a week.

Newer active trap systems, based on an increased understanding of bed bug interactions and chemical communication, are being developed. Two "alarm" pheromones have been identified, specific to bed bugs, and have been incorporated into active traps. They can also be used in part as a control strategy, because they are more effective at attracting bugs. Bedbugs have also been found to use another pheromone to signal gregarious behavior (called a kairomone), which seems to promote aggregation behavior, thereby possibly allowing better control of infestations. Such systems are advertised for $30 for a 90-day supply.

Pest control companies have also used trained canines for bed bug detection. While it is not entirely clear what the dogs are smelling, they presumably are responding to some combination of volatile pheromones or chemicals in bug excrement. These authors found that a trained dog identified live bed bugs, filter paper with a mix of the two

alarm pheromones, and cast skins 100% of the time, although they commented that this was in a clean, well appointed office building. Lower detection rates have been reported when dogs are used in crowded urban settings. One issue with the use of dogs is they may not be able to detect a current infestation from a past infestation, and the dogs can only detect the presence of bed bugs — not reduce their numbers. Newer technologies based on antigens from digested human blood in bed bug feces are also being explored — but again have the disadvantage of not being able to detect current from past infestations. Other technologies based on mass spectrometry, DNA analysis, and electronic noses are accurate but impractical for commercial home use. ■

Pharmacology Update

Ezetimibe and Atorvastatin Tablets (Liptruzet™)

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

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

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

A SECOND EZETIMIBE/STATIN COMBINATION HAS BEEN APproved by the FDA for the treatment of hyperlipidemia. Ezetimibe is now combined with atorvastatin and is marketed by Merck & Co. as Liptruzet.

Indications

Ezetimibe and atorvastatin (EZT/ATO) is indicated as adjunctive therapy to diet to reduce elevated total cholesterol (total-C), LDL-cholesterol (LDL-C), Apo B, triglycerides (TG), and non-HDL-cholesterol (non HDL-C), and to increase HDL-cholesterol (HDL-C) in patients with primary hyperlipidemia or mixed hyperlipidemia.[1] It is also indicated to reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH) as an adjunct to other lipid-lowering treatments.

Dosage

The recommended starting dose is 10/10 mg or 10/20 mg once daily. If a LDL-C reduction of > 55% is required, the recommended starting dose is 10/40 mg once daily. The tablets may be taken any time of the day without regard to meals.

EZT/ATO is available as 10/10 mg, 10/20 mg, 10/40 mg, and 10/80 mg tablets.

Potential Advantages

The addition of EZT to a statin is more effective than doubling the statin dose in terms of LDL-C reduction.[1,2]

Potential Disadvantages

The addition of EZT does not appear to provide incremental benefit on cardiovascular morbidity and mortality.[1]

Comments

EZT/ATO is a new, potent lipid-lowering drug combination. EZT inhibits the absorption of cholesterol at the brush borders of the small intestines and ATO is a potent inhibitor of HMG-CoA reductase. The combination of EZT and ATO has the potential to achieve mean reductions in LDL-C of 61%, total-C 46%, Apo B 50%, TG 40%, and non-HDL-C 58%.[1] The addition of EZT to ATO achieved greater reduction than doubling the dose of ATO. The benefit is greatest at the lower dose. LDL-C reduction achieved with 10/10 mg was 53% compared to 42% for 20 mg ATO. The reductions for 10/20 mg vs 40 mg were 54% and 45%, and 10/40 mg and 80 mg were 56% and 54%, respectively. There does not appear to be additional risk of myopathy or rhabdomyolysis with the addition of EZT.[1] The benefit of EZT beyond lipid lowering is still unclear. A recent Japanese study (n = 243) reported that increasing the dose of ATO (10 mg to 20 mg) can improve endothelial function (assessed by logarithmic-scale reactive hyperemia index), but adding EZT (10/10 mg) resulted in additional LDL-C reduction but no change in endothelial function.[3]

Clinical Implications

The combination of EZT/ATO provides another option for patients with highly elevated plasma lipids to help them achieve target levels. The clinical benefit of the addition of EZT to a statin has been controversial and its routine clinical use questioned.[4] The landmark ENHANCE study showed that the addition of EZT to simvastatin did not reduce the progression of intima-media thickness in the walls of the carotid and femoral arteries in patients with familial hypercholesterolemia compared to simvastatin alone.[5] In contrast, in a population of patients with chronic kidney disease with no history of myocardial infarction or coronary revascularization (Study of Heart and Renal Protection; n = 9270), patients randomized to simvastatin 20 mg plus EZT 10 mg, compared to simvastatin 20 mg, had significant reductions in atherosclerotic events (11.3% vs 13.4%), non-hemorrhagic stroke (2.8% vs 3.8%), and arterial revascularization (6.1% vs 7.6%) during a median follow-up of 4.9 years.[6] Numerically,

the risk of non-fatal myocardial infarction or death from coronary heart disease favored EZT/ATO (4.6% vs 5.0%, $P = 0.37$). In a small pre-post observational study (n = 231), investigators reported a regression in carotid total plaque area 2 years after EZT was added.[7] The definitive clinical benefit of adding EZT to ATO beyond lipid lowering still remains to be determined. ■

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CME Objectives

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

CME Instructions

To earn credit for this activity, follow these instructions:

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. You will no longer have to wait to receive your credit letter! ■

CME Questions

1. The study of measuring blood pressure at every visit vs annual measurement demonstrated that:
   a. every-visit measurement was less sensitive than annual measurement.
   b. every-visit measurement was less specific than annual measurement.
   c. hypertensive adults are younger on average than adults without hypertension.
   d. adults without hypertension are more obese than hypertensive patients.

2. Which of the following is *false* regarding Parkinson's disease?
   a. High-intensity treadmill exercise improves gait speed.
   b. Low-intensity treadmill exercise improves gait speed.
   c. Stretching and strengthening improve gait speed.
   d. Exercise reduces disability in Parkinson's disease.

3. Which of the following factors was associated with a higher risk for cell phone contamination with potentially pathogenic bacteria?
   a. The fact that the user was a physician vs a nurse or other worker
   b. Female gender
   c. The user's having recently cared for a patient with methicillin-resistant *S. aureus*
   d. The fact that the cell phone was a smart phone

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is an advisor for Endo, Kowa, Pricara, and Takeda.

What's the Durability of Lifestyle Change in Type 2 Diabetes?

Source: Jakicic JM, et al. Four-year change in cardiorespiratory fitness and influence on glycemic control in adults with type 2 diabetes in a randomized trial: The Look AHEAD trial. *Diabetes Care* 2013;36:1297-1303.

Embarking on lifestyle change is widely reinforced early on by numerous incidental happenstances. First, response to diet is most prominent in the early weeks of dieting. Second, relative gains in fitness and strength are most obvious in the early weeks of dieting. Third, most support programs providing advisors for diet, exercise, and psychological aspects are "front-loaded" (greater frequency/intensity at first) to try and establish optimum patterns early on. Fourth, as one gains positive initial steps, observers and friends tend to be avid supportive "cheerleaders," a response that diminishes as the going gets tougher, occasional ground is lost, or ground gained is less visible.

Jakicic et al report on the outcome at 4 years in the Look AHEAD Research Group trial. Overweight or obese type 2 diabetics (n = 3942) were randomized to intensive lifestyle intervention (ILI) or standard care. ILI included weekly instructional/support sessions × 24, continuing with lesser (but still frequent) support on diet and exercise throughout 4 years time. Goal exercise time was 175 minutes a week of brisk walking or the equivalent. As perhaps is intuitive, the intervention group achieved and maintained better fitness levels, better A1c, and better weight control. Structured ILI programs can provide sustained benefits in overweight and obese type 2 diabetics. ■

Perimenstrual Asthma: A High-Risk Phenotype

Source: Rao CK, et al. Characteristics of perimenstrual asthma and its relation to asthma severity and control: Data from the severe asthma research program. *Chest* 2013;143:984-992.

Some women with asthma note a worsening of asthma related to onset of menses. In the National Heart, Lung, and Blood Institute Severe Asthma Research Program (SARP), 17% of women (92/483) reported that menses were a trigger for their asthma symptoms. Exploration of perimenstrual asthma (PMA) as a distinct phenotype has been prompted by the recognition of an association between PMA and asthma acuity. Indeed, near-fatal and fatal asthmatic events have been linked to PMA.

Evaluation of women identified with PMA from SARP found that nearly twice as many PMA subjects met criteria for classification as severe asthma than women without PMA. In addition, levels of asthma control were worse in PMA subjects, and they experienced greater urgent health care utilization. Aspirin sensitivity was found three times more often in PMA patients (30% vs 10%), as were nasal polyps (16% vs 5%).

At the current time, PMA is not a widely appreciated entity. In the United States, there are still approximately 5000 asthma deaths per year. Any phenotypic prototype that can help to identify an asthma population at greater risk of fatal or near-fatal asthma might be a step toward reducing the mortality burden of asthma. ■

Risk of New Onset Diabetes with Statins

Source: Danaei G, et al. Statins and risk of diabetes: An analysis of electronic medical records to evaluate possible bias due to differential survival. *Diabetes Care* 2013;36:1236-1240.

The oft-quoted "9% increase in new onset diabetes (NODM) due to statins" sounds pretty scary. What is left out of the aforementioned quote, however, is that the increased risk is a *relative*, not *absolute*, increase. To make the issue more concrete: In one of the largest meta-analyses (n = 91,000), we learned that statins increase risk for diabetes. Among 45,521 statin-treated patients, there were 2226 NODM cases (compared to 2052 of 45,619 placebo recipients); the incidence of NODM then was 4.89% in the statin group, compared to 4.5% in the placebo group, for an underwhelming risk increase of 0.39%. This would translate into a number needed to treat of 250 patients receiving a statin to induce one new case of diabetes. Not nearly so scary, huh?

The most recent analysis of NODM compiled data from the electronic medical records of 500 United Kingdom general practices (n = 285,864). Similar to the above mentioned meta-analysis, the absolute annual incidence in the United Kingdom dataset was 1.59% in statin users compared to 1.13% in nonusers.

Statins can cause NODM, but in trials of secondary prevention, risk of NODM is far outweighed by risk reduction for cardiovascular events. ■

In Future Issues:

n-3 Fatty Acids in Patients with Multiple Cardiovascular Risk Factors

Value of Yoga Training in Paroxysmal Atrial Fibrillation