



# INTERNAL MEDICINE ALERT®

*A twice-monthly update of developments in internal and family medicine*

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## MVP Revisited

### ABSTRACTS & COMMENTARY

**Synopsis:** *The prevalence of MVP is lower than previously reported and the incidence of adverse sequelae is low. MVP defined by new, more specific, echocardiographic criteria is not more common among young individuals with cerebral ischemic events.*

**Sources:** Freed LA, et al. *N Engl J Med* 1999;341:1-7; Gilon D, et al. *N Engl J Med* 1999;341:8-13.

**M**itral valve prolapse (mvp) is believed to be a common disorder that may cause symptoms and lead to valve replacement. However, the true prevalence of MVP in the community setting has not been established since two-dimensional echocardiographic criteria were refined. Thus, Freed and colleagues evaluated the two-dimensional echocardiograms in 3736 unselected subjects participating in the Framingham Offspring Study. Technically inadequate echoes excluded 245 (7%). MVP was analyzed in the parasternal and apical long axis views, and superior displacement of the leaflets greater than 2 mm and at least a 5-mm-thick leaflet were required to diagnose classic MVP. Nonclassic MVP was diagnosed when leaflet thickness was less than 5 mm. MVP was found in 84 subjects (2%): 47 with classic and 37 with nonclassic (1% each).

Complications in the MVP patients included syncope in three, atrial fibrillation in one, stroke in one, one had endocarditis, and one had mitral valve replacement. These incidences of the complications were similar to those without MVP. Most patients with classic MVP had mild mitral regurgitation, whereas those with non-classic and those without had trace regurgitation. Severe regurgitation occurred in 7% vs. 0 vs. 0.5%, respectively. Sixty percent of the MVP subjects were women and MVP subjects were leaner than the others (BMI 24 vs 27;  $P < 0.001$ ). Systolic murmurs and clicks were more prevalent in MVP subjects vs. the others ( $P < 0.001$ ) and were found in about one-quarter of the classic MVP subjects. Symptoms of chest pain and dyspnea were not more frequent in MVP subjects. Freed et al conclude that in a community-based population sample using modern echo criteria, the prevalence of MVP is lower than previously reported and the incidence of adverse sequelae is low.

## INSIDE

*Well-done red meat and breast cancer risk*  
**page 115**

*Oral creatine supplementation*  
**page 116**

*The link of clinical risk factors for epilepsy patients in motor vehicle accidents*  
**page 116**

*Levalbuterol inhalation solution (Xopenex-Sepracor)*  
**page 117**

A higher prevalence of MVP has been reported in young patients with cerebrovascular events, but the true prevalence with modern two-dimensional echocardiographic criteria is unknown. Thus, Gilon and associates used a case-controlled design to evaluate 213 patients 45 years old or younger with ischemic stroke or transient ischemic attacks (TIA) by echocardiography and compared them to 263 controls. Cardiac or vascular causes of the cerebral ischemic event were identified in 142 of the 213 patients; 93 had major vessel disease in the neck and 49 had a cardiac source of embolism. Of the 71 without overt cardiovascular disease, only 16 had no risk factors for cerebral ischemic events. MVP was found in four of the 213 cerebral event cases (2%) and seven of the 263 controls (3%). Interestingly, none of the patients in either group had classic MVP, more than trace MR, or left atrial enlargement. The frequency in the 71 patients without identifiable cardiovascular disease was 3% and none of the 16 without any risk factors for cerebral ischemic events had MVP. Gilon et al conclude that

MVP defined by new, more specific, echocardiographic criteria is not more common among young individuals with cerebral ischemic events as compared to controls.

#### ■ COMMENT BY MICHAEL H. CRAWFORD, MD

These two studies are important because they are the first attempt to re-evaluate MVP in light of the new echocardiographic diagnostic criteria by the investigators who developed the new criteria. Not surprisingly, the prevalence of MVP is much less than previously believed, is similar in men and women, and is evenly distributed over adult ages in Freed et al's study.

Whether 2% is the true incidence in the U.S. population is less certain since the study population is relatively small and homogeneous. Also, this is a cross-sectional study in which only the survivors are evaluated. However, it is free of the sick population selection bias of hospital-based studies. Certainly, the 5-35% incidence of previous reports is erroneous and the true value is probably less than 5%. This is extremely important because a low disease prevalence in a population renders screening tests such as echocardiography useless from a cost-effectiveness point of view. What about patients with symptoms? Wouldn't they have a higher prevalence and make echocardiography more valuable as a screening tool? Freed et al's study indirectly answers this question by documenting that symptoms are no more frequent in the MVP patients than in the others. Also, Gilon et al's study demonstrates that even young patients with cerebral ischemic events do not have a higher incidence of MVP and most of them have other traditional risk factors for stroke. Thus, without other evidence of cardiac disease, nonspecific cardiac symptoms and cerebral ischemic events are not an indication for echocardiography to look for MVP.

Before we close the echo lab, it is still true that MVP is the most common cause of mitral valve surgery in the United States and some patients with MVP do have complications. MVP is a spectrum from normal variants to severe myxomatous changes such as seen in certain hereditary disease such as Marfan's syndrome. Freed et al's study uses an operational classification based upon an arbitrary cutoff of leaflet thickness of more than 5 mm representing "classic MVP." Using this cutoff point confined severe regurgitation almost exclusively to the classic group. Other studies have shown that complications such as heart failure, endocarditis, and the need for surgery are much more common in the classic group. Freed et al showed that mitral regurgitation was usually trivial in the nonclassic MVP and normal subjects but was mild or greater in the classic cases. This suggests that antibiotic prophylaxis may be necessary only in the

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classic cases or those with more than mild mitral regurgitation, but this remains to be proven.

Not surprisingly, the physical examination was not very effective at detecting MVP since it is well known that most cases of mild mitral regurgitation are not detectable by auscultation. However, since the prognosis of patients with mild or less mitral regurgitation is unknown, but presumably largely benign even if they have MVP, echocardiography to detect such patients does not seem cost-effective. In Freed et al's study, complications attributed to MVP were low (6%) and not significantly different from the non-MVP subjects (7%). This study showed that mitral valve clicks and systolic murmurs were more frequent in classic MVP (11% and 22%, respectively) than in nonclassic MVP (8% and 10%) or normals (1.5% and 4%), which was statistically significant ( $P < 0.001$ ). Also, this study confirmed that MVP patients tend to be thinner than normals (BMI 24 vs 27;  $P < 0.001$ ).

Even though MVP is generally benign, the clinician cannot ignore the person with MVP. Most of the subjects with MVP in Freed et al's study would not have gotten an echo outside this protocol because less than one-third would have specific cardiac symptoms or physical findings. The data suggest that the nondetection of these patients is acceptable since their complication rate is low and the detection methods are expensive and will have a low yield if applied broadly. An echo is certainly justifiable in those with specific cardiac symptoms and signs, but not those with cerebrovascular disease and no evidence of cardiac disease. Also, specific cardiac symptoms and signs are more frequent in the classic cases of MVP where complications are more likely. (*Dr. Crawford is Robert S. Flinn Professor, Chief of Cardiology, University of New Mexico, Albuquerque.*) ❖

## Well-done Red Meat and Breast Cancer Risk

ABSTRACT & COMMENTARY

**Synopsis:** *Exposure to heterocyclic amines (or other compounds) formed during high-temperature meat cooking may play an important role in the risk of breast cancer.*

**Source:** Zheng W, et al. *J Natl Cancer Inst* 1998;90:1724-1729.

**H**eterocyclic amines, mutagens formed in meats cooked at high temperatures, have been

demonstrated as mammary carcinogens in animals. A nested, case-control study among 41,386 cohort members of the Iowa Women's Health Study evaluated the potential role of heterocyclic amines and intake of well-done meat in the risk for human breast cancer.

A questionnaire was mailed to individuals who had breast cancer diagnosed during the period from 1992 through 1994 and a random sample of cancer-free cohort members to obtain information on usual intake of meats and on meat preparation practices. Color photographs showing various doneness levels of hamburger, beef steak, and bacon were included. Multivariate analysis was performed on data from 273 case subjects and 657 control subjects who completed the survey.

A dose-response relationship was found between doneness of meat consumed and breast cancer risk. The adjusted odds ratios (ORs) for very well-done meat vs. rare or medium-done meat were 1.54 (95% confidence interval CI 0.96-2.47) for hamburger; 2.21 (95% CI 1.30-3.77) for beef steak; and 1.64 (95% CI 0.92-2.93) for bacon. Women who consumed these three meats consistently very well-done had a 4.62 times higher risk (95% CI 1.36-15.70) than that of women who consumed the meats rare or medium. Risk of breast cancer was also elevated with increasing intake of well-done to very well-done meat.

Consumption of well-done meats, and thus, exposure to heterocyclic amines (or other compounds) formed during high temperature meat cooking, may play an important role in the risk of breast cancer.

### ■ COMMENT BY JOHN La PUMA, MD, FACP

Put another brat on the fire! Here in Chicago, you can hear the backyard grillmeister next door man the tongs, shift the coals, and swear at the cat nearly every weekend and most weeknights. The grill is the one part of the kitchen in which most men feel truly at home, as it is usually not in the kitchen, but on the deck, in the backyard, by the shore, at the beach.

But what to do about the well-done crust, where evil lies? In this study, although frying, grilling, and barbecuing were only weakly correlated with the risk of breast cancer, well-doneness was highly correlated. And well-doneness can come from any of these cooking methods—plus roasting, deep frying, even sautéing.

This is strong, comprehensive, epidemiological case-control data. More than 41,000 Iowa women, aged 55-69, have been assessed for cancer risk and prevalence since they returned a mailed questionnaire in January 1986. No information was collected then about meat or its usual doneness, so the investigators performed a case-control study from 1995-1996. The investigators,

from the Universities of Minnesota and Iowa and the National Cancer Institute, included chicken and fish with the definition of meat, but the correlation was with red meat.

Tell your patients who want to reduce their risk for breast cancer to cook or order their burgers and steak medium or rare, and to send them back or do it over if overdone. This is even more important than reducing red meat intake. If patients or the grillmeister want a good crust, use cracked spices (e.g., peppercorns or cumin seeds) and whole seeds (e.g., sesame or pumpkin) pressed into the meat. These will add extra flavor, so much so that you won't miss the nearly burned char. (Dr. La Puma is Professor of Nutrition, Kendall College, Director, C.H.E.F. Clinic, C.H.E.F. Skills Research, Alexian Brothers Medical Center, Elk Grove Village, Ill.) ❖

## Oral Creatine Supplementation

ABSTRACT & COMMENTARY

**Synopsis:** No evidence is given to support an ergogenic effect of creatine supplements in sporting activities such as running, swimming, or cycling. Potential complications are noted from the use of creatine as a dietary supplement.

**Source:** Juhn MS. *Phys Sports Med* 1999;27(5):47-50ff.

Juhn provides an excellent review of the current thinking with regard to use of oral creatine supplementation to enhance athletic performance. He notes the small number of good scientific articles that exist in the literature. While there is some evidence that these supplements can enhance performance in repeated short bursts of stationary cycling and weightlifting, there is no evidence to support an ergogenic effect on other sporting activities such as running, swimming, or even cycling on the road. He clearly identifies some potential complications from the use of creatine as a dietary supplement. It has been repeatedly shown that a modest weight gain occurs after the typical loading dose is taken over a five-day period and that this weight gain is probably due to water retention and not to an acute gain in muscle mass. Muscle cramping, gastrointestinal complaints, renal dysfunction, and dehydration all have been reported as complications of the use of creatine. The weight gain due to water retention may decrease performance, offsetting any potential ergogenic effect of

the creatine. Juhn concludes this excellent review by stating, "...the evidence that creatine improves running and swimming performance is not convincing...[and]...creatine has not been shown to be ergogenic outside the laboratory setting."

### ■ COMMENT BY JAMES D. HECKMAN, MD

This is an excellent review of a controversial subject. The enthusiastic endorsement of creatine dietary supplements by celebrity athletes has led to their common consumption among athletes at all levels. Juhn provides a comprehensive list of references that will facilitate anyone's study of this subject. The actual number of well-performed clinical studies on the effect of oral creatine supplementation is quite sparse, and little is known about the specific ergogenic mechanisms if, indeed, they do exist. Juhn clearly points out that there have been no studies performed in the pediatric population with regard to the effect of creatine oral supplementation. Yet, young athletes may be more susceptible to the influence of the advertising campaigns and take the supplement despite the fact that there is little or no evidence that it can be helpful. (Dr. Heckman is Professor and Chairman, Department of Orthopaedics, University of Texas Health Science Center, San Antonio, TX.) ❖

## The Link of Clinical Risk Factors for Epilepsy Patients in Motor Vehicle Accidents

ABSTRACT & COMMENTARY

**Synopsis:** Approximately one-third of all patients were noncompliant in following medication, and about another third initially failed to report their seizures to the state's motor vehicle department.

**Source:** Krauss GL, et al. *Neurology* 1999;52:1324-1329.

A variety of social and economic problems face persons with epilepsy, one being the capacity to drive an automobile to work or fulfill various other daily necessities. This report describes factors that influence the probability of some of these patients having automobile crashes. Krauss and associates identified from their large clinic 61 epileptic patients aged 21-70 who had crashed while driving. Eleven of the 61 crashed during their first seizure and were deleted from the study, leaving 50 "crashers" for

### Levalbuterol Inhalation Solution (Xopenex—Sepracor)

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

analysis. The 50 crashers (mean age, 38.5 years) were matched against 50 other epileptic “control” patients (mean age, 39.8 years) from the same clinic. There were 41 males and nine females populating both groups. None of the controls had ever crashed, but all had undergone two or more seizures and were taking medication. Neither type of seizure, years of driving, purposes of driving, nor type of roads differed between the two groups. Crashers, however, differed in several ways from controls. Seizure frequency was 2.9 per month in the crash group compared to 0.6 per month in the controls. The 50 crashers accumulated 74 seizure-related accidents, many causing severe injury and two being fatal. The controls had none. Major injury accompanied 17 crashers, nine others were injured, and two died. Among the crashers, 14 had more than one seizure-related accident. Additional items associated with a high accident rate included: short seizure-free intervals between attacks, a seizure incidence of  $2.6 \pm 1.2$  per month compared to controls with  $0.59 \pm 0.17$  episodes per month.

Favorable items associated with control patients consisted of: 1) long seizure-free intervals lasting  $145 \pm 29$  weeks; 2) possessing reliable auras that always preceded major seizures; 3) having few prior crashes not related to seizures; and 4) having antiepileptic drugs changed, reduced, or withdrawn by their physician (the last point implies satisfactory improvement in the disease, or possible uncertainty of the diagnosis).

It should be mentioned that approximately one-third of all patients, well-controlled or not, were noncompliant in following medication, and about another third initially failed to report their seizures to the state’s motor vehicle department.

#### ■ COMMENT BY FRED PLUM, MD

Krauss et al relate the bad-good outcomes in these 100 epileptic patients. Not surprisingly, they find that the more difficult to control the primary disease, the greater becomes the risk of automobile crashes or other injuries. They quote evidence that epilepsy increases standard accident rates by “only” 1.3-1.9 times. Even these low figures are regrettable. How sad it is for a person to suffer an embarrassing physiological disease, and also to be ashamed to drive or announce his or her disease to others. New pharmacology is only temporizing present therapy. Hopefully, new brain-delivered medication or stimulation can completely repair some of these unfortunate epileptic patients. (Dr. Plum is University Professor, Weill Medical College; Attending Neurologist, New York Presbyterian Hospital.) ♦

The pharmaceutical company sepracor has created a unique niche for itself by focusing on developing Improved Chemical Entities (ICEs), single-isomer or active-metabolite versions of currently marketed drugs. Their objective is to develop new versions of popular drugs with improved side effect profiles, onset of action, or duration of action by purification of racemic mixtures.

They have had development deals with other manufacturers, but the company’s first individual entry in the market is levalbuterol (Xopenex) for the treatment or prevention of bronchospasm. Levalbuterol is the active (R)-isomer of racemic albuterol. The R-isomer is the active bronchodilating component of racemic albuterol and is touted as offering comparable bronchodilation to racemic albuterol with fewer side effects. The drug is only available as liquid for use in nebulizers.

#### Indications

Levalbuterol is indicated for the treatment or prevention of bronchospasm in adults and adolescents 12 years of age and older with reversible obstructive airway disease.

#### Dosage

The usual starting dose is 0.63 mg administered by nebulization three times a day, every 6-8 hours. Patients with more severe asthma or who do not respond adequately to a dose of 0.63 mg may increase the dose to 1.25 mg three times a day.<sup>1</sup>

Levalbuterol is supplied as a preservative-free 3 mL unit-dose of 0.63 mg and 1.25 mg.

#### Potential Advantages

In vitro data indicate that levalbuterol has a greater affinity for the beta-adrenergic receptors than racemic albuterol and has 100 greater affinity than the (S)-isomer.<sup>1,2</sup> The S-isomer of racemic albuterol has been associated with some bronchoconstrictive response to methacholine with chronic use.<sup>3</sup> In a four-week comparative trial of racemic albuterol and levalbuterol (n = 362), lev-

albuterol produced a numerically better (0.84-0.74 L) but not statistically different improvement in FEV<sub>1</sub> (forced expiratory volume in one second). Levalbuterol at 0.63 mg was comparable to 2.5 mg of albuterol—lev-albuterol 1.25 mg being the most potent and albuterol 1.25 mg the least potent.<sup>4</sup> Similar findings were reported in a crossover study in pediatric patients.<sup>5</sup> In the clinical trial of equipotent doses (0.63 mg of levalbuterol and 2.5 mg of albuterol), levalbuterol caused a lower incidence of nervousness at four weeks (2.8% vs 8.1%) and first-dose increase in heart rate (2.4% vs 5.7%).<sup>1</sup>

### Potential Disadvantages

Levalbuterol is available only as a solution for nebulization—not as the more commonly used and convenient metered-dose inhaler or dry powder for inhalation.

### Comments

Many of the drugs are marketed as racemic mixture. Due to the presence of at least one asymmetric center, these mixtures generally comprise a more active isomer (eutomer) and a less active isomer (distomer). The differences in activity result from stereoselective binding of the drug to various macromolecules (e.g., receptors, enzymes). The distomers can vary in their contribution to the pharmacologic effects of the racemic mixture, and these can range from lack of any activity to antagonism, toxicity, or even completely different activity. The example of the latter is quinine and quinidine. In the case of levalbuterol, limited data suggest that the distomer (S-isomer) may have some antagonistic effect on pulmonary function. Results from clinical data indicate that levalbuterol 0.63 mg is comparable to albuterol 2.5 mg, and levalbuterol 1.25 mg produces the greatest improvement in FEV<sub>1</sub>.<sup>4</sup> These results seem to be consistent with the possible antagonistic effect of the distomer.

The average wholesale cost of levalbuterol is \$1.98 per unit-dose vial, which is 10-15% higher than branded albuterol (Proventil or Ventolin) and is more expensive than generic albuterol (\$1.21 per unit-dose vial).

### Clinical Implications

In theory, it appears that levalbuterol may offer some clinical advantage over racemic albuterol; however, in a large clinical trial involving more than 360 patients, the improvement in FEV<sub>1</sub> was not statistically significant after four weeks. Equipotent doses of levalbuterol and albuterol showed a small difference in favor of levalbuterol for certain beta-adrenergic mediated adverse effects. Therefore, the clinical advantage of administer-

ing the pure eutomer over the racemic mixture has not been clearly established. ❖

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3. *The Medical Letter* 1999;41:51-52.
4. Nelson HS, et al. *J Allergy Clin Immunol* 1998;102(6 Pt 1):943-952.
5. Gawchik SM, et al. *J Allergy Clin Immunol* 1999;103(4):615-621.

## CME Questions

### 7. The incidence of echocardiographic mitral valve prolapse in the Framingham Offspring Study is:

- a. 1%.
- b. 2%.
- c. 4%.
- d. 8%.

### 8. Any ergogenic benefit of oral creatine supplementation in running or swimming may be offset by:

- a. obligatory weight gain.
- b. decrease in alkaline phosphatase.
- c. creatine phosphokinase inhibition.
- d. alteration in the performance of fast twitch muscle fibers.

### 9. Which of the following is true about the crashers in the study of epilepsy patients in motor vehicle accidents?

- a. Seizure frequency was 2.9 per month.
- b. Some crashers had more than one seizure-related accident.
- c. Crashers had 74 seizure-related accidents, with two being fatal.
- d. All of the above

### 10. Which of the following statements is false?

- a. Levalbuterol has a greater affinity for the beta-adrenergic receptors than racemic albuterol.
- b. In the clinical trial of equipotent doses, levalbuterol caused a higher incidence of nervousness at four weeks.
- c. Levalbuterol 0.63 mg is comparable to albuterol 2.5 mg.
- d. None of the above

### 11. The usual starting dose of levalbuterol is:

- a. 0.63 mg three times a day.
- b. 0.25 mg three times a day.
- c. 1 mg three times a day.
- d. None of the above

### 12. Which of the following is true regarding the correlation between doneness of meat and breast cancer?

- a. No strong relationship was found.
- b. A dose-response relationship was found.
- c. A relationship was found with barbecuing but not frying.
- d. A stronger relationship was found with beef than with pork.

### Hypoxemia Improves Efficiency of Supplemental Home Oxygen Prescribing

For patients who have resting hypoxemia, supplemental home oxygen (HO<sub>2</sub>) provides significant survival benefits and remains the only intervention proven to prolong the life of patients with COPD. Implementation of HO<sub>2</sub> is costly, ranging from about \$2000-6000 per year, totaling more than \$1 billion annually for our nation. Ferro and associates postulated that use of a clinical pathway for identification and HO<sub>2</sub> treatment of hypoxemic patients would improve the efficiency of HO<sub>2</sub> prescribing.

Study subjects were all patients from the VA medical center of Albany New York, who had been referred for evaluation of need for HO<sub>2</sub> in 1988-1989, 1990-1991, and 1992-1994. The last time period was immediately following implementation of a pathway for HO<sub>2</sub> in this VA hospital system.

Patients needed to demonstrate a PaO<sub>2</sub> of less than 55 (or < 60 with evidence of end-organ hypoxia), or oxygen saturation corresponding to that level of hypoxemia (SaO<sub>2</sub> < 80% = PaO<sub>2</sub> < 55).

The screening protocol to identify potential candidates for HO<sub>2</sub> included any patient with an FEV<sub>1</sub> less than 1000, impaired diffusing capacity, or abnormal lung volume; all these patients were sent for oximetry. Prior to the study, prescriptions for HO<sub>2</sub> were written on a standard prescription, but the intervention included a customized form requiring checking a box documenting compliance with specific prescribing criteria, including plans for follow-up oximetry if patients failed to meet prescribing criteria.

In the year following the clinical pathway institution, there was a 25% decrease in the number of patients treated. Perhaps surprisingly, the total number of deaths decreased during this year, because of fewer deaths from advanced COPD. Ferro et al demonstrate that use

By Louis Kuritzky, MD

of a clinical pathway can improve efficiency of HO<sub>2</sub> use. ❖

Ferro TJ, et al. *J Clin Outcomes Man* 1999;6(6):27-33.

### Oral Androstenedione and Adaptations to Resistance Training in Young Men

Many young men ingest chemicals that they believe, sometimes correctly, enhance muscularity and strength. Androstenedione (ADSTE) is a testosterone precursor produced by the adrenals and converted into testosterone by 17-beta-hydroxysteroid dehydrogenase, an enzyme diffusely distributed throughout body tissues. ADSTE of plant origin has been marketed and is viewed by some as a natural anabolic steroid alternative. To date, no studies have been done in men to assess the effect of ADSTE on plasma testosterone, though a single small trial in women found substantial increases in testosterone following ADSTE ingestion.

In this study, 20 healthy young men consumed either ADSTE or placebo and had blood sampling for effect on free and total testosterone, LH, and FSH. Additionally, men were enrolled in a resistance exercise training program for eight weeks, using weight lifting three days per week.

Single-dose ingestion of ADSTE resulted in a prompt (within 1 hour) and sustained increase in plasma ADSTE, but had no measurable effect on free or total testosterone, LH, or FSH. Similarly, long-term (8 weeks) use of ADSTE produced no significant effect on testosterone. Additionally, no effect, either positive or negative, was seen upon strength or muscle mass.

Unfortunately, ADSTE use was associated with a significant reduction in HDL as well as an elevation of plasma estrogens estradiol and estrone, which have been associated with gynecomastia, as well as other health risks.

King and colleagues conclude that ADSTE does not provide testosterone

enhancement or bolster muscular strength or mass, yet does induce other potentially deleterious changes. ❖

King KS, et al. *JAMA* 1999;281:2020-2028.

### Dietary Hydrogenated Fats on Serum Lipoprotein Cholesterol Levels

Trans-fatty acids are present in meat and dairy products as a result of bacterial fermentation that occurs in ruminant animals. They are also produced during the processing of vegetable oils by hydrogenation, which has been used to convert vegetable oils that are liquid at room temperature to a more solid or semi-solid status. Products like margarine have been widely embraced by the American public in an effort to reduce calories and saturated fat, when compared with using butter. There has been the suggestion that trans-fatty acids are detrimental to serum lipids when compared to cis-fatty acids. The current study evaluated the effect of a variety of forms of margarine and vegetable shortening with diverse levels of trans-fatty acids when substituted for butter in controlled diets.

Men and women older than age 50 (n = 36) who were ostensibly healthy other than having modest elevations of LDL cholesterol (> 130 mg/dL) were fed controlled experimental diets for periods of 35 days. In each diet, 30% of calories were from fat; types of fat substituted included soybean oil, semiliquid margarine, soft margarine, shortening, stick margarine, and butter.

Dietary fat substitution with agents containing the lowest amounts of trans-fatty acids (i.e., soy and semiliquid margarine) were associated with the most favorable changes in LDL, VLDL, and the total cholesterol: HDL cholesterol ratio. Lichtenstein and associates conclude that the current recommendations to consider both the content of trans-fatty acids and saturated fat in dietary planning are appropriate. ❖

Lichtenstein AH, et al. *N Engl J Med* 1999;340:1933-1940.

## Computer Oversight

By Ken Grauer, MD

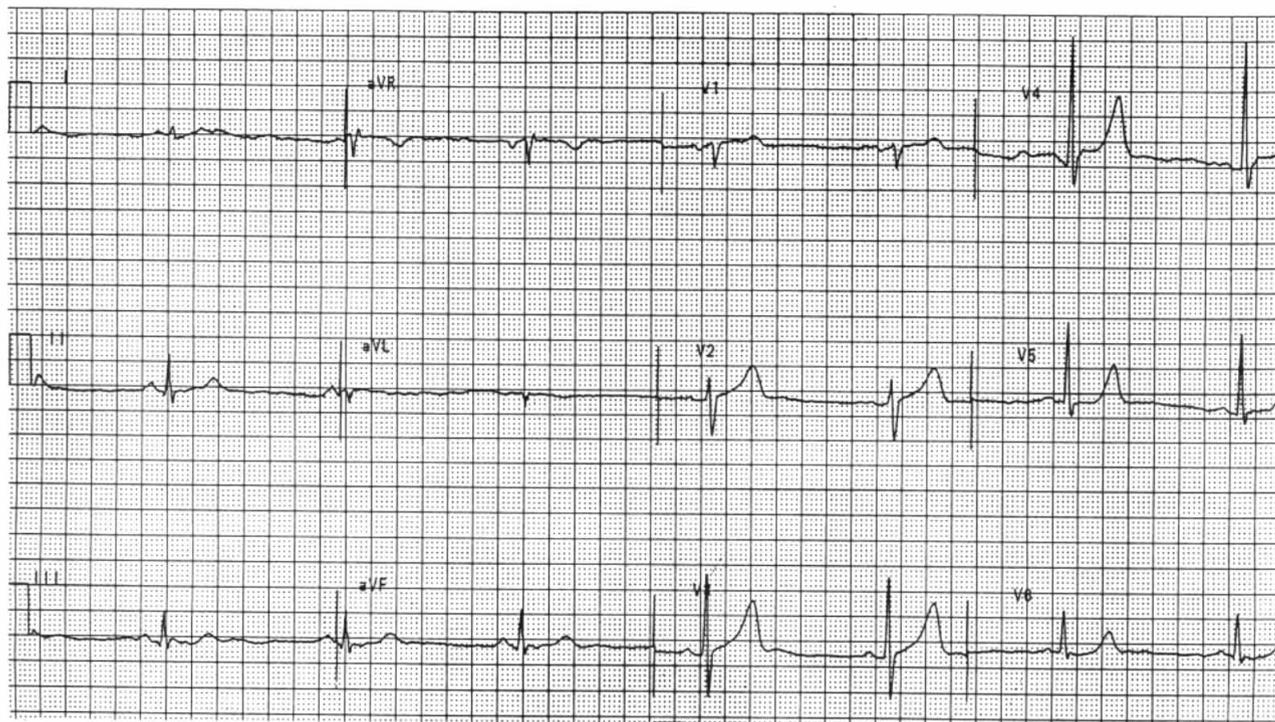


Figure. ECG obtained from a 62-year-old man who was seen in an ambulatory care setting.

**Clinical Scenario.** The ECG shown in the Figure generated a computerized interpretation of "sinus bradycardia—otherwise normal ECG." Do you agree with this interpretation?

**Interpretation.** The rhythm is sinus bradycardia at a rate of 50 beats/minute. The mean QRS axis and all intervals are normal. QRS amplitude is relatively decreased in the standard limb leads. Transition is normal and occurs between leads  $V_2$  and  $V_3$ . There is no sign of chamber enlargement. The most remarkable finding on this tracing is the presence of tall peaked T waves in most precordial leads. In addition, the ST segment is distinctly flat in leads  $V_4$  through  $V_6$ , instead of manifesting the normal smooth upslope with gradual transition into the T wave (as seen in leads  $V_2$  and  $V_3$ ).

Although hyperkalemia is clearly suggested by T

wave appearance in this tracing, serum potassium was not increased. Other than hyperkalemia, T wave peaking in anterior precordial leads may be seen as a normal variant or as a manifestation of posterior wall ischemia.

Anterior leads typically reflect a mirror image view of ischemic events that occur in the posterior wall. The "mirror image" view of T wave peaking would be deep symmetric T wave inversion, or a pattern suggestive of ischemia. In support of the interpretation that T wave peaking in anterior precordial leads might reflect posterior ischemia is the finding of ST segment flattening in lateral precordial leads. Such ST flattening may be a subtle sign of coronary artery disease. Clinical correlation would be needed in this case to determine the relevance of these subtle but suggestive ECG signs of potential ischemic heart disease. ♦

## In Future Issues:

Cigar Smoking and CVD, COPD, and Cancer

Ultrasound Therapy for Calcific Tendonitis