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The Clinical Breast Examination: Are You Doing it Right?

ABSTRACT & COMMENTARY

Synopsis: *A thorough clinical breast examination can detect cancers missed by mammography.*

Source: Barton MB, et al. *JAMA* 1999;282:1270-1280.

Barton and colleagues conducted a pooled analysis of the English literature on the effectiveness and techniques of clinical breast examination. Clinical breast examination screening was compared to a combination of clinical examination and mammography. The reduction in breast cancer mortality rate was similar. This is a strong argument that clinical breast examination alone can have a beneficial effect on the risk of breast cancer mortality. Importantly, all studies have reported a proportion of breast cancers detected by clinical examination alone (3-45% of breast cancers missed by screening mammographies). In other words, a clinical breast examination can detect cancers missed by mammography. The literature on clinical breast examination is plagued by variability. To a significant degree, this is due to the lack of an unstandardized method of clinical breast examination. The accuracy of clinical breast examination is further reduced by not spending sufficent time at the examination, reduced sensitivity in younger more dense breasts, large breasts, and lumpy breasts. Barton et al concluded that there is sufficient evidence to warrant screening clinical breast examination in every woman older than 40 years of age, and that approximately 50% of asymptomatic breast cancers can be detected by a well-performed breast examination.

COMMENT BY LEON SPEROFF, MD

This is an article that every clinician who cares for adult women should read. I have always taken pride in my technique for breast examination and, I suspect, this is true for most clinicians. However, this article revealed to me that my technique is not good enough. After making a convincing argument that the literature supports the value of clinical breast examination for the detection of breast cancer, Barton et al provide a detailed description of a technique based upon the research literature, especially that regarding the development and standardization of

Volume 4 • Number 8 • December 1999 • Pages 57-64

INSIDE

the clinical examination. There are five vital parts to the correct technique for clinical breast examination:

- A systematic search pattern
- Thoroughness with adequate duration
- Varying palpation pressure
- The use of three fingers and the pads of the fingers
- A circular motion of the finger pads

In excellent diagrams, this article describes the best patient position to achieve flattening of the lateral and medial parts of the breast, a requirement that is essential for adequate examination. A circular boundary for the examination is inadequate. A complete examination requires covering a rectangular area, bordered by the clavicle, the mid-sternum, the bra line, and the mid-axillary line. The most effective examination pattern is not the circular pattern I have used but, in fact, a vertical strip pattern or lawn mower technique, beginning in the axilla, moving to the bra line, and then back and forth, overlapping rows. The three middle fingers are held together. Palpation is performed by the pads of the fingers, rotating in small dime-sized circles. Most important, at each position, three levels of pressure should be exerted (light, medium, and deep) to complete palpation of all levels of tissue. The duration of examination affects the accuracy. Studies have demostrated that a careful examination of an average size breast requires at least three minutes. I know I have not been spending six minutes examining both breasts of patients. In one study, it was documented that the average time equaled 1.8 minutes. Of note is the lack of data supporting inspection in various positions. Thus, it is recommended that careful breast palpation should be combined with careful visual examination simultaneously.

Because of this article, I have already changed the technique of my breast examination, especially changing the pattern of palpation and the duration of examination. I urge you to obtain a copy of this article. Not only are the numbers important, but the description of technique with the excellent diagrams will affect your practice. The numbers tell us that doing it right makes clinical breast examination effective and important. The pictures show us the right way to do it. *(Dr. Speroff is Professor of Obstetrics and Gynecology, Oregon Health Sciences University, Portland, Ore.)* ❖

The Hope Trial

ABSTRACT & COMMENTARY

Synopsis: *.Lowering of blood pressure only accounted for a small proportion of the decrease of MI and other end points; individuals in the highest quartile of baseline systolic blood pressure had the greatest risk reduction.*

Source: American Heart Association Annual Scientific Sessions, November 7-10, 1999, Atlanta, GA.

The heart outcomes prevention evaluation (HOPE) trial randomized 9541 high-risk patients to the angiotensin-converting enzyme (ACE) inhibitor ramipril (10 mg/d) or placebo and vitamin E (400 IU/d) or placebo for a mean follow-up period of 4.5 years. This international study was carried out in 267 hospitals and 19 countries, with the majority of patients coming from the United States. The ramipril arm was stopped in early 1999 because of a favorable outcome for the ACE inhibitor; the vitamin E arm has continued. The study population consisted of individuals with documented coronary artery disease (CAD), cerebrovascular, or peripheral vascular disease. In addition, diabetics without vascular disease with at least one additional CAD risk factor were enrolled. All individuals were older than 55 years of age. Patients had no history of heart failure; hypertensives could be enrolled if blood pressure was controlled (46% had hypertension). Thirty-eight percent had diabetes, 11% had a previous stroke, 43% had

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peripheral vascular disease, and two-thirds had an elevated cholesterol level. Eighty-one percent of all patients had CAD, half with a prior myocardial infarction (MI). The results were striking, with a robust 20-25% reduction in relative risk favoring ramipril for all vascular end points. (*See Table*.) There was a 22% reduction in the primary end point of cardiac death, stroke, or nonfatal MI (17.7% vs 14.1%). There was a major decrease in stroke and in new heart failure as well as for revascularization. Of interest, new onset diabetes was decreased by 32% (P = 0.002). New renal dysfunction/dialysis or microalbuminuria was also decreased by ramipril. An echo substudy of approximately half the entire cohort (mean ejection fraction of 60%) demonstrated comparable risk reductions for all end points as the entire cohort. Higher risk patients had a greater reduction in events than those at lower risk. It was concluded that lowering of blood pressure only accounted for a small proportion of the decrease of MI and other end points; individuals in the highest quartile of baseline systolic blood pressure had the greatest risk reduction. The hypertensive and nonhypertensive patients had no difference in benefit from ramipril. Vitamin E had no effect on total mortality, cardiovascular deaths, or other end points.

Table

HOPE	End Points (Ramipril vs Placebo)			
	RAM (%)	**PLAC (%)**	**P Value**	**RR**
CV death, MI, or stroke	14.1	17.7	0.001	0.78
All MI	9.8	12.0	0.0005	0.80
CV death	6.0	8.0	0.0002	0.75
NMFI	5.9	7.5	0.0002	0.78
Revascularization	16.0	18.6	0.001	0.85
All death	10.3	12.2	0.003	0.83
Stroke	3.4	4.9	0.0002	0.68
Nondiabetes	3.7	5.3	0.002	0.68
CHF	9.2	11.7	0.002	0.77

Note: The *New England Journal of Medicine* has taken the unusual step of premature electronic publication of this trial on its electronic website: (http://www.nejm.org/content/yusuf/1.asp).

COMMENT BY JONATHAN ABRAMS, MD

These data have already achieved considerable attention and were formally announced at the European Cardiac Society Meeting at the end of August. The benefits of the ACE inhibitor in individuals who ordinarily would not be treated with such a drug are impressive and concordant with a large amount of vascular biology research, endothelial function studies, and mechanistic hypotheses regarding prevention or slowing progression of vascular disease. These data raise the question as to whether *all* individuals who meet the HOPE criteria should be treated with an ACE inhibitor. Given that the entire cohort had an event rate of cardiac death, stroke, or MI of greater than 3% per year, it seems reasonable that for patients with documented vascular disease, representing the majority of the HOPE cohort, or individuals at high risk for future events (e.g., diabetics with risk factors or those with multiple CAD risk factors), ACE inhibitor therapy should be considered. There is considerable disappointment regarding the antioxidant hypothesis because of the null effects of vitamin E. Earlier data this year from the GISSI-3 trial were also negative in a large population given vitamin E. Some believe that the combination of vitamin E and vitamin C, or the use of different antioxidants, will be necessary to really test the oxidation hypothesis. Certainly, HOPE and GISSI-3 deflate the present enthusiasm for routine use of anti-oxidant vitamins. (*Dr. Abrams is Professor of Medicine, Division of Cardiology, University of New Mexico, Albuquerque*.) ❖

Homocysteine and the Risk of Heart Disease, Stroke, and Death

ABSTRACTS & COMMENTARY

Synopsis: *These studies indicate that hyperhomocysteinemia is an independent risk factor for atherothrombotic disease, although its causal relation to atherosclerosis has not been totally proven.*

Sources: Kark JD, et al. *Ann Intern Med* 1999;131:321-330; Selhub J, et al. *Ann Intern Med* 1999;131:331-339; Eikelboom JW, et al. *Ann Intern Med* 1999;131:363-375; Bostom AG, et al. *Ann Intern Med* 1999;131:352-355; Graham I. *Ann Intern Med* 1999;131:387-388.

In 1969, mccully noted the association between homocystinuria and premature thromboembolic disease[1] and suggested that an elevated plasma homocysteine level might be a cardiovascular risk factor in the general population.[2] Plasma homocysteine levels are determined both by genetic and nutritional factors. Defects in the enzymes that control homocysteine metabolism or deficiencies in vitamin cofactors (folic acid, B_6, B_{12}) can result in elevated plasma homocysteine.

Kark and associates studied a community cohort of 1788 middle-aged and elderly residents of Jerusalem and recorded 405 deaths over a decade. The mortality hazard ratio was 2.0 (95% CI, 1.3-3.0) when the highest and

lowest fifths of the homocysteine distributions were compared. The difference was greater in men than in women. Ten percent of deaths were attributable to homocysteine levels greater than 14 mmol/L. The study found that elevated homocysteine levels were associated with cardiovascular and total mortality.

Selhub and colleagues used a nationally representative sample of 3563 men and 4523 women aged 12 years or older to define reference ranges for total homocysteine levels among persons who were folate and vitamin B_{12} replete and had normal creatinine concentrations. Reference ranges for serum homocysteine concentration increased with age. A high homocysteine concentration was defined as at least 11.4 mmol/L for men and at least 10.4 mmol/L for women. In study participants, two-thirds of cases of high homocysteine levels were associated with low serum concentrations of folate, vitamin B_{12}, or both. However, a low vitamin concentration alone contributed little to the prevalence of high total homocysteine levels in the entire population.

Eikelboom and colleagues reviewed the epidemiologic evidence relating homocysteine to cardiovascular disease. They concluded that although the association between homocysteine and cardiovascular disease is strong, the data from prospective studies do not prove a causal relation. Therefore, the effectiveness of folate and vitamins B_6 and B_{12} in reducing cardiovascular morbidity and mortality requires testing in randomized trials.

Bostom and colleagues examined the association between baseline nonfasting plasma homocysteine levels and incident stroke in 1947 Framingham Study participants of whom 1158 (60%) were women and 789 (40%) were men. The mean age ± SD of the cohort was 70 ± 7 years. Age, systolic blood pressure, current smoking, diabetes, and atrial fibrillation or coronary heart disease were independently predictive of total stroke occurrence. Elevated homocysteine levels also were independently associated with stroke incidence. When quartile 4 (homocysteine level 14.24-219.84 mmol/L) was compared to quartile 1 (homocysteine level 4.13-9.25 mmol/L), the relative risk was 1.82 (*see Table*).

Table

Predictors of Stroke Incidence in the Framingham Study Cohort

Variable	Relative Risk (95% CI)
Age, per one year increase	1.06 (1.04-1.09)
Systolic BP, per 20 mmHg increase	1.16 (1.01-1.34)
Smoking	1.52 (1.03-2.24)
Diabetes mellitus	1.90 (1.25-2.89)
Atrial fibrillation	2.29 (1.29-404)
Coronary heart disease	1.49 (1.04-2.16)
Homocysteine level (quartile 4 c/w quartile 1)	1.82 (1.14-2.91)

Source: Modified from Bostom AG, et al. *Ann Intern Med* 1999;131:352.

COMMENT BY JOHN J. CARONNA, MD

These studies indicate that hyperhomocysteinemia is an independent risk factor for atherothrombotic disease, although its causal relation to atherosclerosis has not been totally proved. Therefore, the practicing physician should measure plasma homocysteine concentration as well as folate and vitamin B_{12} levels as part of risk assessment. It appears that most people with low serum folate or vitamin B_{12} levels also have high homocysteine levels.

In an editorial commenting on several of the articles reviewed above, Graham emphasizes that recommendations about prescribing folic acid or vitamin B_{12} to patients with elevated homocysteine levels must wait for the results of randomized controlled trials.[3] Nevertheless, as he suggests, it is reasonable to prescribe multivitamins and folic acid supplements of 0.4-1.0 mg daily to patients at high risk for cardiovascular and cerebrovascular disease because of the interaction of high homocysteine levels and conventional risk factors. (*Dr. Caronna is Vice-Chairman, Department of Neurology, Cornell University Medical Center; Professor of Clinical Neurology, New York Hospital.*) ❖

References

1. McCully KS, Wilson RB. *Atherosclerosis* 1975;22: 215-227.
2. McCully KS. *Am J Pathol* 1969;56:111-128.
3. Clarke R, Collins RJ. *Cardiovasc Risk* 1998;5:249-255.

Breath-Holding Spells and Iron Deficiency

ABSTRACT & COMMENTARY

Synopsis: *It would seem prudent that children experiencing repetitive breath-holding spells should be studied for iron deficiency and given appropriate therapy for this when present.*

Source: Mocan H, et al. *Arch Dis Child* 1999;81:261-262.

Breath-holding spells are a frequent complaint in pediatric practice. They are clinical

episodes based upon history given by the family as well as direct observation of the spells. Spells are usually defined as stopping of the child's breathing during expiration after a deep inspiration during crying. Spells are classified as cyanotic, pallid, and mixed according to the color of the patient's skin during the spell. It has been estimated that as many as 27% of otherwise healthy children experience breath-holding spells.[1] The cause of breath-holding spells has not been defined[2]; however, an association with iron deficiency anemia has been suggested and reports have described correction of these spells coincident with iron medication.[3]

Mocan and associates from Turkey studied 91 children, 6-31 months of age, with typical breath-holding spells. Studies of iron status included hemoglobin, mean cell volume (MCV) serum iron, and total iron-binding capacity. Other studies included blood sugar serum calcium, ECG, EEG, and skull x-rays. Sixty-three patients with breath-holding spells had concomitant iron deficiency anemia and were treated with oral iron, 6 mg/kg/d for three months. The remaining 28 patients were not treated. Frequency of the spells were assessed. Fifty percent (32/68) patients treated with iron had complete cessation of spells and another 33.3% (21/68) had partial remissions, with at least a 50% decrease in the frequency of spells. In contrast, only 6/28 (21%) of the non-iron-deficient, nontreated patients had complete or partial improvement during three months of observation. Mocan et al acknowledge that they did not measure serum ferritin levels in these children, and it is possible that some of their "non-iron-deficient" children may have had a degree of iron deficiency.

COMMENT BY HOWARD A. PEARSON, MD, FAAP

Breath-holding spells are most frequent in children of the same age group in which iron deficiency is most prevalent. It would seem prudent that children experiencing repetitive breath-holding spells should be studied for iron deficiency and given appropriate therapy for this when present. One might consider a short course of empiric iron therapy even without blood studies. Mocan et al conclude that anticonvulsants are not the treatment of choice for breath-holding spells in infancy. (*Dr. Pearson is Professor of Pediatrics, Yale University School of Medicine.*) ❖

References

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2. Dimaro FJ, et al. *Clin Pediatr* 1990;29:17-24.
3. Daoud AS, et al. *J Pediatr* 1997;130:547-550.

Pharmacology Update

Levalbuterol Inhalation Solution (Xopenex—Sepracor)

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

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.[1]

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.[1,2] The S-isomer of racemic albuterol has been associated with some bronchoconstrictive reponse to methacholine with chronic use.[3] 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_1 (forced expiratory volume in one second). Levalbuterol at 0.63 mg was comparable to 2.5 mg of albuterol—levalbuterol 1.25 mg being the most potent and albuterol 1.25 mg the least potent.[4] Similar findings were reported in a crossover study in pediatric patients.[5] 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%).[1]

Potential Disadvantages

Levalbuterol is available only as a solution for neubulization—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_1.[4] 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_1 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 administering the pure eutomer over the racemic mixture has not been clearly established. ❖

References

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2. Perrin-Fayolle M. *Lancet* 1995;346:1101.
3. *The Medical Letter* 1999;41:51-52.
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5. Gawchik SM, et al. *J Allergy Clin Immunol* 1999; 103(4):615-621.

Attention CME Subscribers

Due to an American Health Consultants error, a mistake has been made with the CME numbering. The numbering should have started over in your November 1999 issue. In the November 1999 issue, questions 16-19 should be questions 1-4. We regret any confusion this may have caused. ❖

CME Questions

5. All of the following statements about clinical breast examination are true *except*:

a. The research literature indicates that clinical breast examination can have an effect on breast cancer mortality even in women younger than 40.
b. The duration of clinical breast cancer duration should be at least three minutes per breast.
c. The accuracy of clinical breast examination is reduced in young women, especially when the breasts are large and lumpy.
d. A significant number of breast cancers missed by mammography are detected by clinical breast cancer examination.

6. Breath-holding spells of infancy:

a. can be diagnosed by appropriate laboratory studies and EEG.
b. are characterized by a cessation of breathing during inspiration.
c. are usually diagnosed by the family history coupled with direct observation when possible.
d. do not usually repond to iron therapy and often require anticonvulsant therapy.

7. An increased incidence of heart disease, stroke, and death is associated with plasma homocysteine levels greater than or equal to:

a. 5 mmol/L.
b. 7 mmol/L.
c. 11 mmol/L.
d. 14 mmol/L.

8. 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

By Louis Kuritzky, MD

Hypoxemia Improves Efficiency of Supplemental Home Oxygen Prescribing

For patients who have resting hypoxemia, supplemental home oxygen (HO_2) provides significant survival benefits and remains the only intervention proven to prolong the life of patients with COPD. Implementation of HO_2 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_2 treatment of hypoxemic patients would improve the efficiency of HO_2 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_2 in 1988-1989, 1990-1991, and 1992-1994. The last time period was immediately following implementation of a pathway for HO_2 in this VA hospital system.

Patients needed to demonstrate a PaO_2 of less than 55 (or < 60 with evidence of end-organ hypoxia), or oxygen saturation corresponding to that level of hypoxemia (SaO_2 < 80% = PaO_2 < 55).

The screening protocol to identify potential candidates for HO_2 included any patient with an FEV_1 less than 1000, impaired diffusing capacity, or abnormal lung volume; all these patients were sent for oximetry. Prior to the study, prescriptions for HO_2 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 oximetries 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 of a clinical pathway can improve efficiency of HO_2 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-betahydroxysteroid 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 semisolid 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.

Lateral Infarction? No *and* Yes!

By Ken Grauer, MD

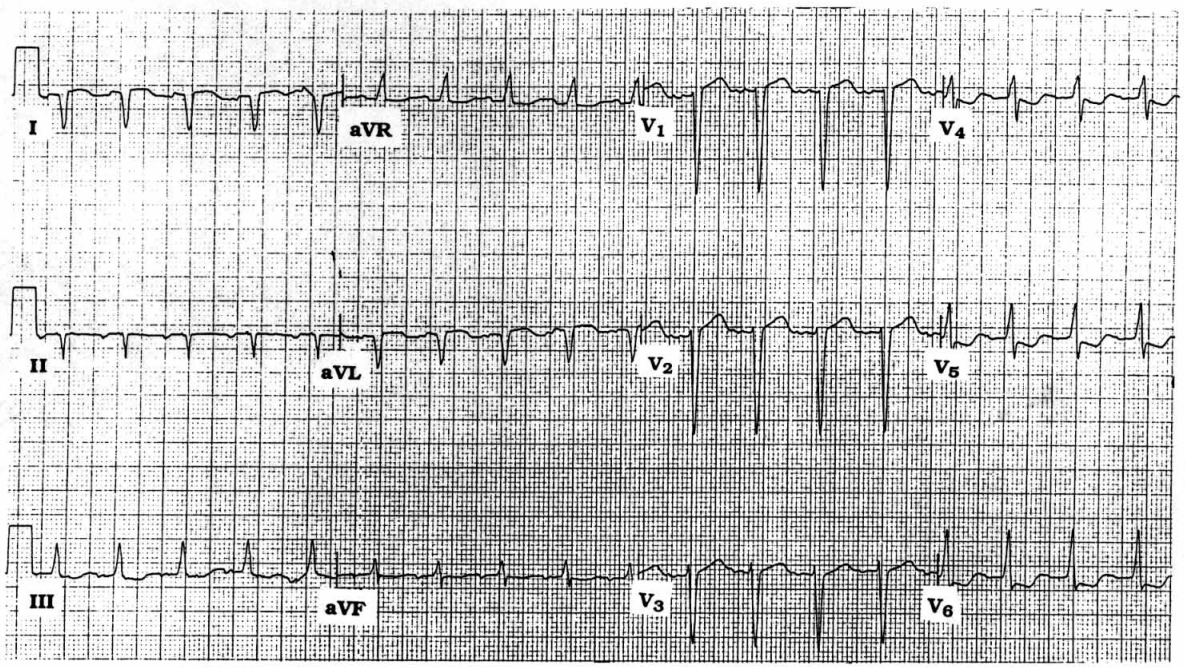

Figure. ECG obtained from a 63-year-old woman with atypical chest pain.

Clinical Scenario: The ECG shown in the Figure was obtained from a previously healthy 63-year-old woman with atypical chest pain. The answer to the question we raise in the title of this ECG Review (*is there lateral infarction?*) is no *and* possibly yes! Can you explain?

Interpretation: There are several unusual findings on this tracing. The first of these becomes evident when assessing the rhythm: P waves are *not* upright in lead II. Although atrial activity is not readily discernible in lead I, the negative QRS complex and T wave in this lead—in association with the upright QRS complex in right-sided lead aVR (a lead which should normally show complete negativity) strongly suggest either dextrocardia or lead misplacement as the cause of the unusual pattern. Normal R wave progression in the precordial leads rules out the former (since dextrocardia would result in *reverse* R wave progression). Confirmation of lead misplacement as the cause of this pattern is easily forthcoming by repeating the ECG after verifying that all limb leads are correctly placed. The deep Q waves (QS complexes) in leads I, II, and aVL disappeared, and a normal upright P wave was seen in lead II on repeat ECG.

Precordial leads are *unaffected* by limb lead misplacement. Thus, the worrisome ST segment sagging depression that is present in leads V_4 through V_6 of the Figure was unchanged on repeat ECG, suggesting a possible acute coronary syndrome. There is, therefore, *no* evidence of lateral infarction from inspection of leads I and aVL (because lead misplacement negates the meaning of the findings in these leads)—but ST depression consistent with possible acute infarction is present in the lateral precordial leads. ❖

In Future Issues:

Empiric Treatment of Pneumonia