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Improvement of Gastroesophageal Reflux Symptoms after Radiofrequency Energy

ABSTRACT & COMMENTARY

Synopsis: *Despite the absence of meaningful clinical trials, the FDA has approved the Stretta™ endoscopic radiofrequency application technique for treatment of gastroesophageal reflux disease (GERD) as of the year 2000. This study demonstrated that this procedure did lead to lessened GERD-related symptoms but not to any decrease in esophageal acid exposure or medication use.*

Source: Corley DA, et al. *Gastroenterology*. 2003;125:668-676.

For obscure reasons, medical device approvals are far less rigorous than FDA approvals for drugs. As a result, the Stretta procedure (radiofrequency applied to the region of the LES) was approved primarily on the basis of relative apparent safety along with the suggestion that results might be more or less equivalent to historical data from fundoplication. There was (and is) no requirement for direct comparison to a placebo or to any active treatment (such as a proton pump inhibitor). The Stretta procedure involves placement of a balloon across the cardioesophageal junction and "cooking" the submucosa with needles affixed to an inflated balloon. Unlike the study that led to approval of the device itself, the present study did compare the radiofrequency technique to endoscopy without intervention (a sham procedure). Step-up therapy was re-instituted after medication withdrawal 21 days postprocedure. Data were available for 56 of 64 patients. Baseline data were similar between the treatment and the control groups. Although symptoms and quality of life were improved after active intervention, there were no statistical differences in PPI use, acid exposure, LES pressure, or the presence of endoscopic esophageal erosions. Complications of the procedure included chest pain, nausea and vomiting, and an episode of bleeding from esophageal ulceration. Oddly enough, a significant number of patients were able to withdraw medications after the sham procedure.

COMMENT BY MALCOLM ROBINSON, MD, FACP, FACG

Although Corley and colleagues put a favorable "spin" on the

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data, most observers would find this study less than compelling. Several experts have suggested that the Stretta procedure may actually "work" by altering visceral sensation rather than by any other effect on GERD or its acid-related pathophysiology. From the perspective of this reviewer, this procedure is not suitable for wide application. In the long run, it seems likely to be relegated to the same "dustbin" as the Angelchick prosthesis for GERD or gastric freezing for ulcer disease. Device regulation should be strengthened to mirror the rigor of the FDA approval process for drugs. As of now, radiofrequency treatment in GERD still needs to be assessed in comparison to one or more of the fine options that exist for medical and surgical management of GERD. ■

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Breast Cancer and HRT: The Million Woman Study

ABSTRACT & COMMENTARY

Synopsis: *Current users of estrogen or estrogen-progestin combinations were shown to have a significantly higher risk of developing and dying from breast cancer. The findings confirm and extend those published last year by the Women's Health Initiative.*[1]

Source: Million Women Study Collaborators. Breast cancer and hormone replacement therapy in the Million Women Study. *Lancet*. 2003;362:419-427.

THE MILLION WOMAN STUDY WAS UNDERTAKEN between the years 1996 and 2001, during which time 1,084,110 UK women provided information about their use of hormone replacement therapy (HRT), as well as other personal details, and were then followed for cancer incidence and death. The participants in the study represent approximately 25% of the UK women in this age group. Approximately half of the women reported current or past use of HRT. During the 5 years of study there were 9364 incident invasive breast cancers and 637 breast cancer deaths after an average of 2.6 and 4.1 years of follow-up, respectively. Current-users of HRT at recruitment were more likely than never-users to develop breast cancer (adjusted relative risk, 1.66 [95% CI, 1.58-1.75; P < .0001) and die from it (1.22 [1.00-1.48]; P = .05). However, past-users of HRT were not at an increased risk of incident or fatal disease (1.01 [0.94-1.09] and 1.05 [0.82-1.34], respectively). Incidence was significantly increased for current-users both of preparations containing estrogen only (1.30 [1.21-1.40]; P < .0001) or estrogen-progestin (2.0 [1.88-2.12]; P < .0001), but the magnitude of the associated risk was substantially and significantly greater for estrogen-progestin than for other types of HRT (P < .0001). When looked at separately, relative risks were significantly increased for users of oral, transdermal, and implanted estrogen formulations (P < .0001). In current-users of each type of HRT the risk of breast cancer increased with increasing total duration of use. Ten years use of HRT was estimated to result in 5 (95% CI, 3-7) additional cancers per 1000 users of estrogen-only preparations, and 19 (15-23) additional cancers per 1000 users of estrogen-progestin combinations.

■ COMMENT BY WILLIAM B. ERSHLER, MD

This large epidemiologic study confirms the associa-

tion of HRT and breast cancer. Furthermore it demonstrates an increased risk for all types of HRT, including estrogen alone or transdermal formulations. The estrogen-progestin combinations seem to be the most dangerous with regard to the development of breast cancer. The duration of HRT use appears to be important, and those current users having been treated for a decade or more were at particularly high risk. To put these findings in perspective, among women from developed countries who never used HRT the incidence of invasive breast cancer is estimated to be typically 32 in every 1000 between the ages of 50 and 65.[2] The cumulative incidence of breast cancer per 1000 associated with different patterns of use of HRT, calculated by applying the relative risk estimates determined in this study to the estimated incidence rates in never-users of HRT, showed that by 5 years use of HRT, beginning at the age of 50, it would be estimated to result in 1.5 additional breast cancers by the age of 65 among 1000 users of estrogen-only preparations, and 6 (CI, 5-7) additional cancers per 1000 users of estrogen-progestin combinations. By 10 years the use is estimated to result in 5 (CI, 3-7) additional cancers in 1000 users of estrogen only, and 19 (CI, 18-20) additional cancers in 1000 users of combined HRT. Looked at another way, use of HRT by UK women, age 50-64 years, in the most recent decade is estimated to have resulted in an extra 20,000 incident breast cancers.

Thus, the cumulated data from this and other well-constructed studies[1, 3-5] indicate an irrefutable association between breast cancer and HRT use. The estimated increased numbers are of great consequence, and physicians need to be aware and to discuss these increased risks if patients are to undertake such treatment approach. The new evidence of breast cancer mortality dictates an explicit position for general practitioners—HRT should be discouraged and, for women presenting with new postmenopausal related health problems, general practitioners should seek alternative solutions. With the current data, it is difficult to find fault with that recommendation. ■

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Dr. Ershler is an Oncologist at the INOVA Fairfax Hospital Cancer Center, Fairfax, VA; Director, Institute for Advanced Studies in Aging, Washington, DC.

Fish Story or Food for Thought?

ABSTRACT & COMMENTARY

Synopsis: *Dietary intake of n-3 fatty acids and weekly consumption of fish may reduce the risk of incident Alzheimer's disease.*

Source: Morris MC, et al. *Arch Neurol*. 2003;60:940-946.

This study examined whether consumption of fish had any effect on the risk of developing Alzheimer's disease. Morris and associates carried out a prospective study of 815 people aged 65-94 in a biracial community in Chicago. Subjects were followed for an average of 4 years for the development of Alzheimer's disease. The subjects completed a dietary questionnaire on average 2.3 years before clinical evaluation of incident disease. The Alzheimer's disease was diagnosed using a structured neurological examination and standardized criteria. A total of 131 people in the sample developed Alzheimer's disease. Participants who consumed fish once per week had a 60% less risk of Alzheimer's disease as compared to those who rarely or never ate fish (relative risk, 0.4). This was in a model in which other risk factors were statistically adjusted to correct for the effects of age, sex, ethnicity, education, stroke, hypertension, heart disease apolipoprotein E genotype, total caloric intake, and consumption of other fats and vitamin E. The association was particularly marked for intake of long-chain n-3 polyunsaturated fatty acids and docosahexaenoic acid (Omega-3). The intake of a-linolenic acid, which is found in vegetable oil and nuts, was protective only in people with the APOe4 allele. Morris et al suggest that the consumption of Omega-3 fatty acids, which are found in fish, vegetable oils, and nuts, may reduce the risk of Alzheimer's disease.

■ COMMENT BY M. FLINT BEAL, MD

This is an interesting study. It is consistent with other studies from Morris et al in another population. The effect size is very large. Whether this will be reproducible in other epidemiological studies remains to be seen, but it is definitely worthy of further investigation. Morris et al have also shown recently that intakes of saturated fat and transunsaturated fat are positively associated with risk of Alzheimer's disease, whereas intakes of W6 polyunsaturated fat and monounsaturated fat are inversely associated. This study was carried out in the same population, and it was shown that persons in the

other upper fifth of saturated fat intake had a 2.2-fold increased risk as compared with persons of the lowest fifth in intake of developing Alzheimer's disease.[1]

Another study of the intake of total fat, saturated fatty acids, transfatty acids, cholesterol and low-intake monosaturated acids, and N6 polyunsaturated acids and N3 polyunsaturated fatty acids was carried out in the Rotterdam epidemiological study. In this cohort of 5395 subjects there was no association between fat intake and subsequent development of dementia.[2]

If fish intake is indeed protective against Alzheimer's disease, what could be the mechanism? It has been shown that long-chain n-3 polyunsaturated fatty acids have an effect on membrane stability, as well as neurite health outgrowth. They could potentially alter b-amyloid processing. Omega-3 fatty acids have previously been shown to be associated with a lower risk of cancer, as well as cardiovascular disease and stroke. A protective dose effect of fish intake against stroke was detected in the Nurse's Health Study, as well as in the Health Professional Follow-up Study. However, in this study there was no dose effect. It is conceivable that fish intake could have some minor deleterious effects due to methylmercury and the accumulation of PCBs, which occur in some large predatory fish. Nevertheless, the overall evidence suggests that intake of fish may exert protective effects against a number of diseases and further investigation of its role in protecting against Alzheimer's disease is certainly warranted. ■

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Dr. Beal is Professor and Chairman, Department of Neurology, Cornell University Medical College, New York, NY.

Doctor, I'm Dizzy!

ABSTRACT & COMMENTARY

Synopsis: *Dizziness and vertigo are among the most common complaints seen by neurologists, and benign paroxysmal positional vertigo (BPPV) is one of their most frequent causes.*

Source: Baloh RW. *N Engl J Med*. 2003;348:1027-1032.

Differentiating central from peripheral causes of vertigo is a recurrent clinical challenge that behooves reinforcement. Bedside examination usually suffices, based on the characteristics of the nystagmus, the presence of associated symptoms (or their absence), and results of the head-thrust test. In contrast to centrally originating nystagmus, which is purely unidirectional (horizontal, vertical, or rotational) and which changes direction with change in direction of gaze, nystagmus of peripheral origin is typically horizontal with a rotational component, does not change direction with change in gaze, and demonstrates a positive head-thrust test. Centrally caused vertigo often precludes standing upright without assistance, whereas patients with peripheral vertigo can stand, though they will lean to the side of the lesion. In association with an otherwise normal neurological examination, these characteristics permit a confident diagnosis of peripherally originating vertigo precluding the necessity for expensive imaging procedures. Electronystagmography and audiography are even less rarely required.

Performance of the head-thrust test is straightforward. Have the patient hold his head forward but looking 10° to one side and ask him to continuously fixate on your nose. Quickly jerk the head slightly to that side and watch for corrective saccades. Repeat with the eyes looking to the opposite side. If corrective saccades are present, they indicate that the eyes are moving with the head rather than fixating on the nose and are a sign of vestibulopathy. If the "catch-up" saccades occur with the eyes in one direction but not the other, you have documented an ipsilateral peripheral vestibular lesion, either in the labyrinth or eighth nerve.

Prolonged vertigo, lasting hours to days when associated with unilateral hearing loss, suggests labyrinthitis, labyrinthine infarction, or perilymph fistula. In the absence of hearing impairment, prolonged vertigo suggests vestibular neuritis (neuronitis), whereas in association with neurologic signs and symptoms brainstem or cerebellar infarction is to be considered. Vertigo in Ménière's disease rarely lasts longer than 4-5 hours and is associated with hearing loss, which, however, may not be present initially.

Vertigo is best treated acutely with antihistamines (promethazine, dimenhydrinate, meclizine), anticholinergic or antidopaminergic agents, or GABA-enhancing agents (diazepam, lorazepam). Intramuscular or intravenous administration may be necessary due to the nausea commonly accompanying vertigo. Recovery is otherwise spontaneous, although dizziness and a sense of imbalance may last for weeks to months. Vestibular exercises, including eye-and-head coordination and balance exercises, should begin as

soon as possible as they may shorten the recovery period. Antiviral agents and prednisone are of no proven benefit and long-term use of antihistamines should be avoided as they interfere with the central compensation mechanisms needed for recovery.

COMMENT BY MICHAEL RUBIN, MD

Dizziness and vertigo are among the most common complaints seen by neurologists, and benign paroxysmal positional vertigo (BPPV) is one of their most frequent causes. Resulting from otolithic debris in the lumen of, most commonly, the posterior semicircular canal, BPPV may be easily cured in the majority of instances by the Epley[1] or Semont[2] maneuvers. Regardless of the maneuver chosen, additional enhancements such as mastoid vibration or post-treatment positional restriction adds little. Significantly, neither patient age nor duration of symptoms affects treatment outcome, and the maneuver is recommended even in the elderly with long-standing symptoms.[3] Furthermore, the Semont maneuver benefits patients with a typical BPPV history even in the absence of demonstrable nystagmus on Dix-Hallpike testing.[4] Overall, 90% of BPPV patients benefit, but there is a 50% 5-year recurrence rate,[5] underscoring the importance of self-treatment. Radtke's modified Epley procedure[6] is preferred (more effective) than Brandt-Daroff exercises.[7]

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Dr. Rubin is Professor of Clinical Neurology, New York Presbyterian Hospital-Cornell Campus, New York, NY.

Pharmacology Update

Testosterone Buccal System (Striant)

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

The FDA has approved the first transbuccal delivery system for testosterone replacement therapy in men. Like injection and transdermal testosterone preparations, transbuccal testosterone bypasses hepatic first-pass metabolism that limits the use of oral preparations. The patented delivery system is called Bioadhesion Delivery System. Transbuccal testosterone is marketed by Columbia Laboratories as Striant.

Indications

The testosterone buccal system is indicated for replacement therapy in males with deficiency or absence of endogenous testosterone. These include primary hypogonadism (congenital or acquired), testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. It is also indicated for secondary hypogonadism including hypogonadotropic hypogonadism (congenital or acquired), idiopathic gonadotropin or LHRH deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation.[1]

Dosage

The recommended dose is 1 buccal system (30 mg) placed in the gum region twice daily, morning and evening about 12 hours apart.[1] The system should be placed just above the incisor tooth and application should be alternated between each side of the mouth. It should be held firmly in place with a finger over the lip and against the product for 30 seconds. If the buccal system is dislodged from the gum surface during the 12-hour period a new system should be applied. If the system is dislodged within 4 hours of the next dose the new system should be applied and remain in place until the next scheduled dosing.[1]

Testosterone buccal system is available as 30-mg units.

Potential Advantages

This transbuccal delivery system provides an alternative to the patches, gel, or injectable testosterone formulations.

Potential Disadvantages

The most common side effects reported in the phase III 12-week trial were gum or mouth irritation (9.2%), gum tenderness or pain (3.1%), bitter taste (4.1%), gum edema (2%), headache (3.1%), and taste perversion (2%).[1] Four of 98 patients (4.1%) discontinued treatment due to gum- or mouth-related adverse events.[1]

Comments

Striant is the newest delivery system for testos-

terone. The tablet is placed in the natural depression where the gum meets the upper lip above the incisor teeth. The small, gel-like monoconvex tablet adheres to mucosal surface and remains over a 12-hour period. Testosterone is released and absorbed into the systemic circulation bypassing the liver (ie, first-pass metabolism).[2] Mean total testosterone levels produced by Striant are within normal physiologic range (mean average concentration ranged from 520 to 550 ng/dL) and are similar to those produced by other testosterone formulations such as the patch, gel, and injection.[1,3] FDA approval was supported by a phase III, open-label, parallel, 12-week study with 98 study subjects. Most common side effects were gum irritation, pain, edema or tenderness, mouth irritation, bitter taste or taste perversion, and headache. Gum irritation generally resolved in 1-8 days and gum tenderness in 1-14 days.[1] The wholesale cost for Striant is about $5 per day and similar to that for the transdermal system (eg, Androderm) and the gel (eg, AndroGel).

Clinical Implications

Striant offers another option to the delivery of testosterone. Current formulations include Intramuscular injection, transdermal delivery systems (scrotal and nonscrotal), and topical gel. Bioavailability is poor orally due to poor solubility and extensive first-pass metabolism. Low testosterone levels have been associated with muscle atrophy and weakness, osteoporosis, increase in fat mass, depression, and sexual dysfunction. Some uses of testosterone replacement, however, are controversial and are often fueled by patient demand. In a recent survey about 90% of members of the American Association of Clinical Endocrinologists were concerned about potential abuse of testosterone.[4] The decision to treat often comes down to a benefit vs risk analysis, not so much in truly hypogonadal young men but more so with older men with normal or low-normal testosterone levels. A recent review suggests that testosterone replacement is warranted in older men with a significant decline in testosterone level regardless of symptoms and those with mildly decreased testosterone levels with symptoms of hypogonadism (eg, osteoporosis, sexual dysfunction). Potential risks include increased incidence of sleep apnea, stimulation of previously unseen prostate cancer, and elevation of prostate-specific antigen (PSA).[4] There has been no study longer than 3 years.[3] The Institute of Medicine has been called upon to help design a large-scale trial to help clarify these important issues. ■

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CME Questions

10. The Stretta™ procedure for endoscopic treatment of reflux disease can be expected to accomplish which of the following objectives?

a. Normalization of esophageal acid exposure
b. Improved lower esophageal function
c. Decreased heartburn symptoms
d. Healing of esophageal erosions
e. Avoidance of any significant procedure-related symptomatic complications

11. Vertigo of a peripheral cause would be expected to:

a. be purely unidirectional (horizontal, vertical, or rotational).
b. change direction with change in direction of gaze.
c. demonstrate a positive head-thrust test.
d. All the above
e. None of the above

12. The risk for developing breast cancer is increased for women (aged 50-65 years) who are currently using which of the following HRT preparations?

a. Oral estrogen
b. Oral estrogen-progestin combinations
c. Transdermal estrogen
d. Implanted estrogen
e. All of the above

Answers: 10 (c); 11 (c); 12 (e)

Correction

The correct answer for CME question #9 in the August 29 issue, "***Which of the following statements about nonvalvular atrial fibrillation is true?***" is selection "e": ***There is wide variation in the rate of warfarin treatment by patient age and insurance status.*** Selection "a" was inadvertently given as the correct answer. We regret any confusion this may have caused. ■

By Louis Kuritzky, MD

Urinary Tetrahydroaldosterone as a Screen for Primary Aldosteronism

It has recently been suggested that a substantial minority of persons with hypertension—as many as 1 out of 7 or 8—suffer overlooked primary hyperaldosteronism (PHA) as an etiology. Although unprovoked hypokalemia, when present, is a useful stimulus to direct investigation toward PHA as a cause, the inconsistency of this finding, coupled with the frequency of other equally rational explanations for hypokalemia present in hypertensive patients (eg, diuretic therapy), conspire to obscure the diagnosis.

A variety of biochemical diagnostic tests have been used to establish the diagnosis of PHA, including plasma renin-to-aldosterone ratio, plasma aldosterone concentration, 24-hour urinary aldosterone-18-glucouronide, and free aldosterone. Abdelhamid and colleagues sought to prospectively compare the measurement of 24-hour urinary tetrahydroaldosterone (THA), a primary hepatic metabolite of aldosterone, with other commonly used diagnostic measures in a population (n = 1976) of hypertensives, compared to controls.

The diagnostic test with the best sensitivity (96%) and specificity (95%) for PHA was THA, which compared very favorably with plasma aldosterone (89% and 90%), 24-hour urinary free aldosterone (87% and 91%), plasma aldosterone-to-renin ratio (85% and 85%), and even the combination of the latter 2 tests (82% and 85%). Based upon these data, Abdelhamid et al suggest that THA is the appropriate initial best diagnostic test; in the uncommon scenario of a false-negative THA, measuring urinary free aldosterone and aldosterone-18-glucuronide would discover essentially all of the other PHA cases. ■

Abdelhamid S, et al. Am J Hypertens. 2003;16:522-530.

Finasteride and Prostate Cancer

It is apparent that androgenic hormones, in particular dihydrotestosterone (DHT), are participants in the generation of prostate cancer (PCA). Since 5-alpha-reductase inhibitors (5ARI) like finasteride (Proscar) and dutasteride (Avodart) are well demonstrated to reduce levels of DHT and have a favorable effect on the progression of BPH, the idea that such agents might also favorably affect development of PCA has been conceptually appealing for several years.

In the Prostate Cancer Prevention Trial, men aged 55 years or older (n = 18,882) with normal digital rectal examination (DRE) and serum PSA (< 3.0 ng/mL) were randomly assigned to either 5ARI (finasteride) or placebo and followed for 7 years. Men underwent prostate biopsy if an abnormal DRE or PSA elevation (> 4.0 ng/mL) occurred during follow-up. For men who were receiving 5ARI, the PSA was appropriately adjusted (measured PSA multiplied by 2.3) due to the well-known PSA-reducing effect of 5ARI treatment.

PCA was found in 18.4% of the 5ARI group, as opposed to 24.4% of the placebo group, indicating a statistically significant 25% reduction in prevalence. PCA with high Gleason scores (ie, highly aggressive) were seen significantly more frequently in the 5ARI than placebo group (37% vs 22%), but overall there was a net reduction in all PCA. Erectile dysfunction, reduced ejaculate volume, loss of libido, and gynecomastia were more frequent in the 5ARI group; BPH and related symptoms, urinary retention, need for invasive prostate procedures, and UTI were more frequent in the placebo group. Finasteride has been demonstrated to prevent or delay the onset of PCA; for men who seek clinician's advice on such treatment, it will be important to acknowledge the slight increase of aggressive PCA tumor incidence and other potential adverse effects that need to be weighed in the risk benefit analysis. ■

Thompson IM, et al. N Engl J Med. 2003;349:215-224.

Impermeable Bed Covers in Patients with Allergic Rhinitis

Sufferers of allergic rhinitis (ALR) are often sensitive to a variety of allergens, of which house-dust mites are a commonplace troublemaker. The 2 most common offending house-dust antigens, *Dermatophagoides pteronyssinus* and *D farinae*, are readily measured in samples of dust from floors and fabric. Although numerous environmental control measures have been advocated for patients with dust and mold allergy, their efficacy in producing symptom reduction is only scantily supported.

This trial included patients with ALR (n = 279) who were randomly assigned to impermeable bedding covers (which reduce house-dust mite populations) vs standard coverings (placebo). Outcomes measured included concentrations of house-dust mite antigens, as well as clinical symptoms, over 12 months' observation.

Despite reductions in concentration of house-dust mite antigen, no clinical ly meaningful improvements in ALR symptom scores were seen. Because substantial amounts of time, energy, and economic resources are spent upon environmental manipulation for persons with allergy, these negative outcomes should stimulate reappraisal of the role of tools like impermeable mattress covers in the management of AR. ■

Terreehorst I, et al. N Engl J Med. 2003;349:237-246.

Concealing the Cause

By Ken Grauer, MD

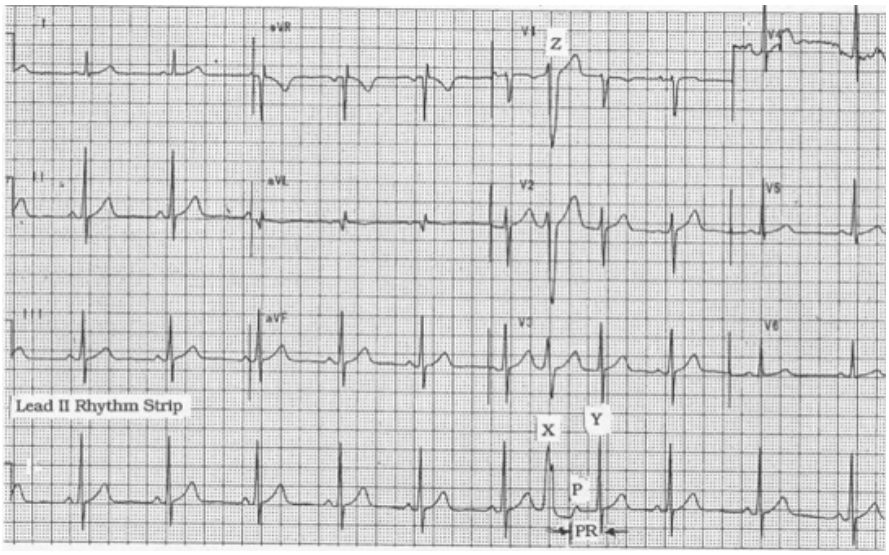

Figure. 12-lead ECG and rhythm strip obtained from an otherwise healthy 53-year-old man.

Clinical Scenario: The 12-lead ECG and accompanying rhythm strip in the Figure were obtained from an asymptomatic and otherwise healthy 53-year-old man. What two things are unusual about the beat marked X? Did first degree AV block suddenly develop for the following sinus-conducted beat (beat Y)?

Interpretation: The ECG in the Figure shows normal sinus rhythm. With the exception of the beat marked X and an isolated Q wave in lead aVL that is probably incidental, this is essentially a normal tracing.

The beat labeled X in the rhythm strip is a PVC (premature ventricular contraction). The first somewhat unusual aspect of this beat is its morphology, as suggested by its appearance in simultaneously recorded leads V_1, V_2, and V_3. The RS pattern of this PVC in lead V_1 (beat Z) is consistent with a LBBB (left bundle branch block) morphology. While far from infallible, PVCs that manifest a "LBBB-like" morphology (deep S wave in lead V_1; tall monophasic R wave in leads I and V_6) are more likely to be of right ventricular origin. This is a less common origin of ventricular ectopy than the left ventricle, which tends to produce PVCs with a predominantly positive deflection in lead V_1.

The most interesting aspect of the beat labeled X in the rhythm strip is that this PVC is *interpolated*. PVCs most often occur in the cardiac cycle at a point that prevents conduction of the next sinus impulse. This is because the ventricles are refractory to normal conduction immediately after the PVC. As a result, PVCs are usually followed by a short pause. The ventricles usually recover in time to conduct the next normally occurring P wave.

On occasion, a PVC may occur at just the right point in the cardiac cycle that allows the ventricles to recover sooner, and therefore in time to be conducted by the P wave that immediately follows the PVC. Thus, the PVC labeled X is interpolated. Instead of a pause, the next QRS complex (beat Y) occurs nearly on time. Note that although the P wave immediately following the PVC (labeled P) also occurs on time, its PR interval (ie, the PR interval preceding beat Y) is prolonged compared to all other PR intervals on the rhythm strip. This reflects the phenomenon known as "concealed" conduction, in which the PVC (beat X) partially conducts back toward the AV node enough to prolong conduction of the next sinus impulse (the P wave labeled P). There is no AV block. The clinical significance of interpolated PVCs is the same as that of any other PVC—which is negligible as an isolated occurrence in an asymptomatic and otherwise healthy adult. ■

In Future Issues: Omeprazole for Bleeding Ulcers