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Cholesterol and Stroke

ABSTRACT & COMMENTARY

Synopsis: *Pravastatin reduced strokes/TIAs in postmyocardial infarction patients with average cholesterol levels despite concomitant use of antiplatelet agents by most of the patients.*

Source: Plehn JF, et al. *Circulation* 1999;99:216-223.

The relationship between cholesterol levels and stroke is controversial. The Cholesterol and Recurrent Events (CARE) trial is the first secondary prevention trial of "statins" after myocardial infarction (MI) that included stroke as a secondary end point. The 4159 patients in this study had average cholesterol levels (mean 209 mg/dL) and LDL levels (139 mg/dL). The primary end point of reduction in cardiac events was reduced 24% in the pravastatin vs. placebo patients. Also, strokes were reduced 32%. The patients were well matched and antiplatelet drug use was 85% in each group. Pravastatin lowered cholesterol 20%, LDL 32%, and triglycerides 14%; HDL was raised 5%. Strokes or TIAs occurred in 92 patients on pravastatin and 124 on placebo—a 27% reduction. There was no increase in intracerebral hemorrhage on pravastatin and no difference in fatal strokes (6 total). Subgroup analysis showed equally beneficial effects for groups based on age, sex, hypertension, smoking, left ventricular ejection fraction, and baseline lipid levels. Plehn and colleagues conclude that pravastatin reduced strokes/TIAs in postmyocardial infarction patients with average cholesterol levels despite concomitant use of antiplatelet agents by most of the patients.

COMMENT BY MICHAEL H. CRAWFORD, MD

Stroke following MI is mainly cardioembolic in the early recovery phase (< 3 months) but is more ischemic later due to the relationship between coronary and cerebrovascular disease. The CARE patients were randomized from three to 20 months (mean 10) postinfarction and only 15% of the strokes were considered embolic. However, the benefit was observed in all types of strokes. The reduction in stroke/TIA rates paralleled the reduction in coronary events, but the point where the event curves separated between the groups was different: 3.5 years for stroke and about 1.5 years for coronary

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events. Similar results were seen with the 4S secondary prevention study, with a 30% stroke reduction starting after three years. Although the percent reduction is impressive, the P value was not robust at 0.02, but considering that 85% of patients were on antiplatelet drugs, the results are noteworthy.

The mechanism of pravastatin's benefit is unknown, but a relationship was noted with serum LDL levels; the higher the level, the more the benefit. Stroke reduction was a nonsignificant 14%, with LDL less than 125 mg/dL and 54% with LDL more than 150 mg/dL ($P < 0.001$). However, in the West of Scotland primary prevention trial of patients with similar lipid levels, but no prior MI, stroke reduction was an insignificant 11% despite similar reductions in cholesterol on pravastatin treatment. Thus, the mechanism of stroke reduction may involve effects of the statins beyond lipid lowering. Also, the West of Scotland study suggests that the results of this trial in postmyocardial infarction patients may not be transferable to patients with less disease. Whatever the mechanism, it appears that stroke reduction should be another expected benefit of lowering LDL cholesterol in postmyocardial infarction patients with LDL more than 130 mg/dL. (*Dr. Crawford is Robert S. Flinn Professor, Chief of Cardiology, University of New Mexico, Albuquerque.*) ❖

Which is most correct concerning stroke postmyocardial infarction?

a. Almost all are cardioembolic.
b. They are independent of cholesterol levels.
c. Beta blockers reduce their incidence.
d. Statin therapy reduces their incidence.

Role of Inhaled Corticosteroids in Stable Chronic Obstructive Pulmonary Disease

ABSTRACT & COMMENTARY

Synopsis: *A meta-analysis of the original data sets of randomized controlled trials in patients with moderately severe COPD showed a beneficial effect on FEV1 during two years of treatment with daily doses of inhaled corticosteroids.*

Source: van Grunsven PM, et al. *Thorax* 1999;54:7-14.

Chronic obstructive pulmonary disease (copd) is common and there is an increasing worldwide prevalence. It affects an estimated 15 million Americans and is the fourth most common cause of death in the United States. Despite an improved understanding of the disease, treatment has changed little over the past 20-30 years and COPD remains a major health problem worldwide. Smoking is the major risk factor for COPD, accounting for some 90% of cases. There are no available treatments proven to prevent or slow the progression of airflow obstruction in COPD other than smoking cessation. However, improved understanding of the molecular and cellular mechanisms involved has led to the identification of a variety of inflammatory mediators and proteases that contribute to the lung injury in COPD. Whether anti-inflammatory agents could alter the course of COPD by blocking these pathways is not known.

Inhaled corticosteroids are recognized as an effective anti-inflammatory therapy in asthma, and their early introduction is recommended by national and international guidelines. Since asthma and COPD have many features in common, it has been hypothesized that steroids should be effective in COPD. However, the only trials that have shown unequivocally positive results were those that did not exclude asthmatics. Studies of steroid use in COPD that used stringent criteria for the diagnosis of COPD have shown substantial short-term benefit in 15-30% of subjects. Similarly, trials of steroids during exacerbations of COPD have yielded more

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impressive results than in stable disease, suggesting that steroid response in individual patients may vary with time and/or circumstance. The role of inhaled corticosteroids in the long-term management of COPD is still unclear.

A Medline search of papers published between 1983 and 1996 was performed and three studies were selected, two of which were published in full and one in abstract form.[3-5] The primary question was: "Are inhaled corticosteroids able to slow down the decline in lung function (FEV1) in COPD?" The secondary questions were: "What is the point in time when inhaled corticosteroids start to have a significant effect on the course of lung function?"; "Is there a dose effect relationship?"; and "Which clinical characteristics predict the effect?"

van Grunsven and colleagues have carefully described their inclusion criteria that are based on most recent guidelines for COPD and excluded patients with "asthmatic features" from the original data. They addressed some of the shortcomings of the previous studies by including patients who were likely to have unequivocal COPD for reanalysis. Ninety-five of the original 140 patients treated with inhaled corticosteroids (81 with 1500 mcg beclomethasone daily, 6 with 1600 mcg budesonide daily, and 8 with 800 mcg beclomethasone daily) and 88 patients treated with placebo (of the initial 144 patients) were included in the analysis. The effect on FEV1 was assessed by a multiple repeated measurement technique in which points of time in the study and treatment effects (inhaled corticosteroids compared with placebo) were investigated.

No baseline differences were observed (mean age 61 years, mean FEV1 45% predicted). The estimated two years difference in pre-bronchodilator FEV1 was +0.034 1/year (95% confidence interval [CI] 0.005-0.063) in the inhaled corticosteroid group compared with placebo. The post-bronchodilator FEV1 showed a difference of +0.039 1/year (95% CI -0.006 to 0.084). No beneficial effect was observed on the exacerbation rate. In the treatment group, six of the 95 subjects dropped out because of an adverse effect that may have been related to the treatment compared with two of the 88 patients in the placebo group. Worsening of the disease was the reason for dropout in four patients in the treatment group compared with nine in the placebo group.

COMMENT BY ALAN M. FEIN, MD

The role of steroids in stable COPD is not yet settled. The current COPD guidelines recommend use of steroids only in patients who show objective benefit during a steroid trial.[1,2] This rationale implies that there are two kinds of patients with COPD: those who do respond to steroids and those who don't. The advent of inhaled steroid preparations has substantially lowered the risk of steroid therapy. Faced with a COPD patient in whom the treatment options with clear-cut benefit are limited, the use of inhaled steroids, a treatment that is judged to be safe, has become widespread in the absence of definite evidence of benefit.

Clearly, this interesting study approach has limitations that must be considered when accepting van Grunsven et al's conclusions. Some of the data points were obtained by interpolation, as measurement intervals during the follow-up in one of the trials were two-monthly rather than three-monthly.[4] No effect of smoking status was seen contrary to previous reports, as steroids may not protect the bronchial wall of the host against bacterial colonization, the beneficial effects on FEV1 with inhaled steroids were not accompanied by a lower number of exacerbations, which is thought to be due to bacterial super-infection. Contrary to general opinion, the use of beta-agonists did not have a deleterious effect on the progression of COPD in this study.

Despite its shortcomings, the most important finding of this study is that the use of high-dose inhaled steroids reduced the observed rate of decline in FEV1 by approximately 34 mL/year in patients with moderately severe COPD. The rate of decline in FEV1 in a COPD population is approximately 50-60 mL per year, with most rapid declines exceeding 80 mL per year. Survival in COPD correlates inversely with FEV1, and treatment that slows the accelerated decline in FEV1 might reduce mortality.

Different dosages of inhaled corticosteroids were used, although it is unlikely that this would affect the data as a majority of the patients received high-dose treatment. A large European trial of inhaled steroids in patients with mild COPD (EUROSCOP) has been presented, but not published, and has reportedly failed to show a distinct effect on lung function, which may be due to the low dose of inhaled corticosteroid (800 mcg budesonide). Two large European studies, the Copenhagen City Lung study (800-1200 mcg budesonide in mild COPD) and ISOLIDE (1000 mcg fluticasone in severe COPD) is about to be completed. Together, these results should give us a clear picture of the long-term effects of inhaled steroids in large groups of patients with COPD.

We presently stand on the threshold of a considerable increase in data concerning inhaled steroids in COPD. This study has provided clear evidence that inhaled corticosteroids may reduce the rate of decline in FEV1 in moderately severe COPD, but a number of unanswered issues remain, such as: optimal dose, duration of treatment, time course of action, and long-term side effects. ❖

The meta-analysis of long-term effects of inhaled corticosteroids in chronic obstructive pulmonary disease showed that:

a. use of inhaled steroids was accompanied by a lower number of exacerbations.
b. use of beta-agonists had a deleterious effect on the progression of COPD.
c. use of high-dose inhaled steroids reduced the observed rate of decline in FEV1.
d. there was a decrease in the prevalence of smoking.

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Nutrition Alerts

Vegan Diet and Rheumatoid Arthritis

Source: Nenonen MT, et al. *Br J Rheumatol* 1998;37: 274-281.

We tested the effects of an uncooked vegan diet, rich in lactobacilli, in rheumatoid arthritis (RA) patients randomized into diet and (omnivorous) control groups. The intervention group experienced subjective relief of RA symptoms during intervention. Return to an omnivorous diet aggravated symptoms. Half of the diet patients experienced adverse effects (nausea or diarrhea) during the three-month diet and withdrew from the experiment prematurely.

Indicators of RA activity did not differ statistically between groups. The positive subjective effect experienced by patients was not discernible in objective measures of disease activity (Health Assessment Questionnaire, duration of morning stiffness, pain at rest, and pain on movement). However, a composite index showed a higher number of patients with between three and five improved disease activity measures in the intervention group. Stepwise regression analysis showed a decrease in disease activity with three factors: intake of lactobacilli-rich and chlorophyll-rich drinks; an increase in fiber intake (mean 42 g daily); and no need for gold, methotrexate, or steroid medication ($r2 = -0.48$, $P = 0.02$). Subjects also lost 9% of their body weight on average, and increased their daily protein intake from 58 g to 80 g daily.

Nenonen and colleagues from the Helsinki National Research and Development Center for Welfare and Health, tested a "living food" or uncooked vegan diet. Seeds, grains, and fermented products, together with their processing, characterize a "living food" diet, as does the absence of animal products, added salt or raffinated (conventionally sweetened) substances.

Both diet and control groups were prohibited from having caffeine, chocolate, and alcohol, and no one was taken off medication. Patients with the best adherence had the least objective disease activity, but adherence was a problem. Only five or six of the 19 (mean age 49; 18 women) who completed the diet intervention drank their 0.5-1 liter of fermented wheat and wheatgrass drink daily. Eight dropped out because of nausea; three dropped out because of diarrhea. The fermented wheat bacteria supplied the lactobacilli; the wheatgrass drink was not analyzed.

Specific foods are often linked with RA symptoms. Though Nenonen et al note that RA patients' intestinal flora appear to differ from that of healthy subjects, it is unclear from this analysis why fermented and uncooked products may be useful in RA.

Creative chefs might help Nenonen et al and their subjects. Good cooks can make almost anything taste good, even without cream, butter and salt, though those are like stethoscopes, reflex hammers, and tongue depressors to doctors. But there's no cooking here. Just fermenting.

It's impossible to tell whether the fiber, the relatively high protein level, the lactobacilli, the weight loss, the wheatgrass, or something else was completely responsible for the modest subjective effect.

For RA patients who are truly committed to changing their symptoms and can stick to an extreme diet, a living food diet may be worth a short, time-limited trial. These results warrant better quality future research and more work in the kitchen. (*This Nutrition Alert was written by John La Puma, MD, FACP, Adjunct Professor of Nutrition, Kendall College; Director, C.H.E.F. Clinic C.H.E.F. Skills Research, Alexian Brothers Medical Center, Elk Grove Village, IL.*) ❖

Different Diet, Less Gas?

Source: King TS, et al. *Lancet* 1998;352:1187-1189.

King and associates examined whether colonic malfermentation could be a factor in the pathogenesis of Irritable Bowel Syndrome (IBS). Six

female IBS patients and six female controls were enrolled in a randomized, cross-over study in which subjects received either a standard diet (containing the usual Western foods) or an elimination diet for two weeks, followed by the alternate diet for two weeks after a two-week washout period. The elimination diet included fish and meat, but not beef, soya products replaced dairy products, and cereals other than rice were prohibited. There were also restrictions on yeast, citrus, caffeine, and tap water.

Toward the end of each two-week diet, fecal excretion of fat, nitrogen, starch, and nonstarch polysaccharide was measured, along with a 24-hour indirect calorimetry.

On the standard diet, colonic gas production of hydrogen was two times higher in IBS patients than controls, and excretion of hydrogen plus methane was nearly four times higher. While both IBS and control subjects had reduced gas production, especially of hydrogen while receiving the elimination diet, the IBS patients had near-normalization of their gas excretion patterns. This was associated with significant improvement in their gastrointestinal symptoms. King et al speculated that the elimination diet favorably alters the activity of certain bacteria, thereby decreasing symptoms of IBS. (*This Nutrition Alert was written by Carol A. Kemper, MD, Clinical Assistant Professor of Medicine, Stanford University.*) ❖

Pharmacology Update

Miglitol Tablets (Glyset-Pharmacia Upjohn)

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

Pharmacia upjohn recently began marketing the second alpha-glycosidase inhibitor, miglitol (Glyset), joining acarbose in this class. These drugs are not hypoglycemic agents; rather, they inhibit carbohydrate digestion in the brush border of the gut, delaying the absorption of glucose that attenuates postprandial hyperglycemia.[1,2] Miglitol and acarbose were both developed by Bayer. Miglitol was approved by the FDA in 1996 and subsequently licensed to Pharmacia Upjohn.

Indications

Miglitol is indicated as monotherapy as adjunct to diet to improve glycemic control in patients with type 2 diabetes whose hyperglycemia is not adequately managed with diet alone. It is also indicated in combination with a sulfonylurea when diet plus a sulfonylurea or sulfonylurea alone does provide adequate glycemic control.

Dosage

The recommended starting dose is 25 mg three times daily with the first bite of each meal. Due to gastrointestinal side effects, some patients may start with 25 mg once daily and gradually increase to three times daily. The suggested titration regimen is 25 mg at the start of dinner for two weeks, 25 mg at breakfast and dinner for two weeks, then 25 mg three times a day at each meal. Patients should remain on 25 mg three times a day for 4-8 weeks. The dose should then be increased to 50 mg three times a day for about three months. Hemoglobin A1c should be measured periodically to assess the effectiveness of the drug. If the response is inadequate, a dose of 100 mg three times a day may be considered. If no improvement in glycosylated hemoglobin is observed, a reduction in the dose should be considered. The usual maintenance dose is 50 mg three times a day.[1]

Should a patient experience hypoglycemia (e.g., when miglitol is used with a sulfonylurea), glucose, not sucrose (table sugar), should be used to correct this condition since miglitol will inhibit the breakdown and absorption of sucrose.

Miglitol is supplied as 25 mg, 50 mg, and 100 mg tablets.

Potential Advantages

Similar to acarbose, miglitol does not cause hypoglycemia, hyperinsulinemia, or weight gain. When used with sulfonylureas, alpha-glycosidase inhibitors enhance glycemic control as well as attenuate sulfonylurea-associated weight gain and postprandial serum insulin concentrations.[2] An unpublished 24-week study provided by the manufacturer suggests that miglitol is more potent than acarbose on a mg basis. Miglitol at 50 mg three times daily produces similar reduction in glycosylated hemoglobin as 100 mg three times daily of acarbose. An even greater reduction was achieved with miglitol 100 mg three times a day.[1]

Potential Disadvantages

Gastrointestinal side effects are common with alpha-glycosidase inhibitors. In U.S.-based placebo-controlled trials, the incidence of GI side effects compared to placebo were: flatulence (41.5% vs 12%),

diarrhea (28.7% vs 10%), and abdominal pain (11.7% vs 4.7%). Flatulence is primarily caused by the gas production resulting from the metabolism of unabsorbed carbohydrates by the intestinal microflora. In these trials, the incidence of discontinuation due to adverse events was 12% compared to 7% for placebo. Low serum iron was reported in 4.3% of the patients treated with miglitol compared to 2.4% for placebo.[2] In contrast to acarbose, miglitol is a smaller molecule (molecular weight of 207 vs 646) and shows dose-dependent systemic absorption. A 25 mg dose is completely absorbed while a 100 mg dose is 50-70% absorbed.[2] The significance of this systemic absorption is not known. However, since miglitol is excreted primarily by the kidneys, its use in patients with renal impairment is not recommended. Miglitol is less effective than sulfonylureas in reducing glycosylated hemoglobulin. Reduction in glycosylated hemoglobulin is generally 25-50% less than that achieved with a sulfonylurea.[3,4] Miglitol is contraindicated in patients with inflammatory bowel disease, colonic ulceration, predisposition to intestinal obstruction, and chronic intestinal disease associated with digestion or absorption disorder.[1]

Comments

Alpha glucosidase inhibitors, such as acarbose and miglitol, inhibit membrane-bounded intestinal brush border alpha glucoside hydrolase enzymes. This action inhibits the breakdown of dietary polysaccarides to absorbable monosaccarides resulting in a blunting of postprandial glucose excursion. Several placebo-controlled trials have demonstrated that miglitol significantly reduces glycosylated hemoglobin and one-hour postprandial glucose levels compared to placebo.[1] The placebo-subtracted reduction of HbA1c ranged from 0.26% to 0.81% with doses of 25 mg to 100 mg three times a day with a study duration of three months to one year. One-hour, placebo-subtracted, postprandial glucose levels were reduced by 28 to 87 mg/dL. Compared to a sulfonyurea, miglitol was about 25-50% less effective in terms of reduction in HbA1c.[3,4] The addition of miglitol to a sulfonylurea resulted in additional reduction of HbA1c by 0.30 to 0.82%.[2] Two recently published one-year studies reported that miglitol was efficacious in Hispanics as well as African-Americans with type 2 diabetes.[5,6] Gastrointestinal side effects and frequent dosing (with each meal) are potential limitations for adherence with dosing regimens. Efficacy has also been reported in the elderly and also in type 2 patients treated with insulin.[4,7] The potential advantages of alpha glucosidase inhibitors are lack of hypoglycemia, hyperinsulinemia, and lack of weight gain. Unpublished data suggest that miglitol may be more potent than acarbose. The clinical relevance of significant systemic absorption of miglitol is not known.

The daily wholesale cost ranges from $1.50 to $2 per day and is similar to that of acarbose.

Clinical Implications

Miglitol provides another option for the management of diabetes mellitus. These drugs may be considered for monotherapy in newly diagnosed mild type 2 diabetics and as adjunctive therapy with oral agents or insulin in type 2 patients, especially where weight gain or hyperinsulinemia are problematic. ❖

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Which is *not* true about miglitol?

a. It does not cause hypoglycemia when used as monotherapy.
b. If used in combination therapy, sucrose should not be used to treat hypoglycemia.
c. It does not need to be titrated.
d. It may attenuate sulfonylurea associated weight gain.

Readers are Invited

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By Louis Kuritzky, MD

Prevalence and Extent of Atherosclerosis in Adolescents and Young Adults

The pathobiological determinants of Atherosclerosis in Youth (PDAY) Study reports atherosclerosis in 15- to 34-year-old men and women who underwent autopsy. Since fatty streaks and fibrous plaques commonly begin in this age group, the process of progressive lipid deposition, proliferation of smooth muscle, and ultimate mortal plaque rupture can be assessed in autopsy population studies.

The study included information from almost 3000 subjects, detailed primarily from pathologic evaluation of the thoracic aorta, abdominal aorta, and coronary arteries. As anticipated, the mean area involved and prevalence of atherosclerosis increased with age. The PDAY study showed that fatty streaks in the abdominal aorta and right coronary artery tend to be replaced with raised lesions like fibrous plaque and complicated atherosclerotic lesions.

Traditionally established risk factors were related to the progression from fatty streak to more complicated and more high-risk lesions. VLDL and LDL levels were directly associated with fatty streaks and raised lesions; HDL levels were indirectly associated with these lesions. Obesity, smoking, elevated glycohemoglobin levels and hypertension were all associated with the negative pathologic arterial changes in these young men and women that we see reflected later as cardiovascular mortal and morbid end points. Strong and colleagues conclude that true primary prevention of atherosclerotic disease will have to begin prior to adolescence. ❖

Strong JP, et al. JAMA 1999;281: 727-735.

Level of Physical Activity and the Risk of Radiographic and Symptomatic Knee OA in the Elderly: The Framingham Study

Osteoarthritis (oa) of the knee has sometimes been described as "wear and tear" arthritis, alluding to the belief that joint stress induces the observed degenerative changes. Consonant with this opinion is the observation that obesity is associated with knee OA; also, some physically demanding occupations are associated with knee OA. On the other hand, long-distance runners have not been subject to increased risk of OA, and aerobic conditioning exercises have been shown to be therapeutic for knee OA.

The Framingham study began in 1948 in Framingham, MA, with a cohort of 5000 individuals. In examinations no. 18 (1983-1985) and no. 22 (1992-1993), knee radiographs were obtained.

An association between number of hours per day in heavy physical activity and radiographic evidence of knee OA was apparent in men and women; more than four hours daily heavy physical activity was associated with a greater than six-fold increased risk of radiographic knee OA. Heavy physical activity was exemplified by such activities as mowing with a nonpower mower, shoveling, digging, chopping wood, and brisk cycling. On the other hand, there was no association with light or moderate physical activity, daily amount of walking, or number of stairs climbed. Symptomatic knee OA was also associated with heavy physical activity. Obese individuals were disproportionately at high risk. McAlindon and associates conclude that elderly persons should be advised of the risks involved with heavy activity, particularly if they are obese. ❖

McAlindon TE, et al. Am J Med 1999;106:151-157.

Sustained Release Bupropion, a Nicotine Patch, or Both for Smoking Cessation

Among the 20 million smokers who attempt cessation each year, more than 90% fail to maintain abstinence for longer than one year. Even in patients who use nicotine patches or gum, only 20-30% will remain nonsmokers long term. Seven-week courses of bupropion have demonstrated as much as 23% efficacy at 12 months for smoking cessation. In this placebo-controlled study, Jorenby and colleagues compared sustained release bupropion (n = 244), nicotine patch (n = 244), and the combination of the two (n = 245).

Bupropion was dosed at 150 mg for the first three days, followed by 150 mg bid for nine weeks; nicotine patches were dosed as 21 mg daily for six weeks, followed by 14 mg daily for one week, then 7 mg daily for one week.

Successful abstinence at one year was achieved by 35.5% of the combination therapy group, compared with 30.3% in the bupropion alone group, and 16.4% in the nicotine patch alone group.

Weight gain, a daunting deterrent to cessation for many smokers, occurred in all groups but was least in the combination treatment group (1.1 kg over 7 weeks). Adverse events caused medication discontinuation in less than 10% of subjects.

In this trial, the combination of bupropion with nicotine patches demonstrated a trend toward greater efficacy than bupropion alone, with less weight gain at seven weeks. ❖

Jorenby DE, et al. N Engl J Med 1999;340:685-691.

What is Beat X?

By Ken Grauer, MD

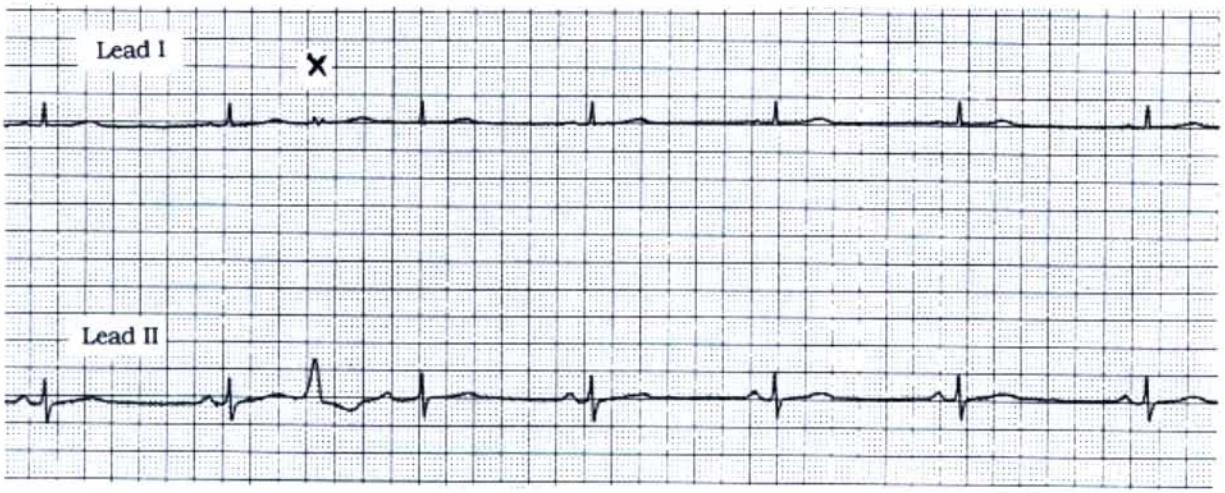

Figure. Simultaneous rhythm strip recording of leads I and II. What is beat X?

Clinical Scenario: The Figure shows a rhythm strip with *simultaneously* recorded leads I and II. What is beat X? What is unusual about this beat? Why is the PR interval of the following beat prolonged?

Interpretation: The underlying rhythm is sinus bradycardia and arrhythmia. Beat X is a premature ventrucular contraction (PVC). Although the amplitude of this beat is greatly reduced (and easy to overlook) in lead I, confirmation of its true etiology is readily apparent from inspection of simultaneously recorded lead II, where this beat is obviously wide and very different in appearance from normal sinus complexes. QRS amplitude in a given lead may be null (or almost so, as in this case) when the mean vector of a beat is oriented perpendicular to the lead being monitored.

The second unusual aspect of beat X is that there is no compensatory pause following this beat, as usually occurs because the premature ventricular complex renders the AV node refractory to conduction of the next sinus impulse. Instead, the R-R interval containing the PVC in this tracing is barely longer than the R-R interval of the underlying sinus rhythm. Such PVCs are said to be "interpolated." The final finding of interest is the presence of *concealed* conduction, which produces PR interval prolongation in the beat following the PVC (seen best in lead II). The term concealed conduction is used when an ECG finding is seen that is not explained by the surface ECG. Instead, one has to postulate that the reason the PR interval of the third sinus beat is prolonged reflects the greater amount of time needed for the atrial impulse to penetrate an AV node rendered partially refractory from the proceding ventricular beat. ❖

In Future Issues:

A National Survey of End-of-Life Care for Critically Ill Patients

Does a Drink a Day Really Keep the Doctor Away?

Bedtime Insulin Plus Metformin Prevents Weight Gain and Reduces Frequency of Hypoglycemia in Type 2 Diabetes