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Addition of Alendronate to Ongoing HRT in the Treatment of Osteoporosis: A Randomized, Controlled Trial

ABSTRACT & COMMENTARY

Synopsis: *In postmenopausal women with low bone density on hormone therapy, the addition of alendronate leads to further increases in bone density.*

Source: Lindsay R, et al. *J Clin Endocrinol Metab* 1999;84:3076-3081.

This study sought to determine if the concurrent use of the bisphosphonate, alendronate, and standard doses of hormone replacement therapy (HRT) would yield greater bone mineral density (BMD) than the use of HRT alone. A total of 428 postmenopausal women with BMD less than two standard deviation (SD) below the mean for a reference population of young women and who had used HRT for at least one year were randomized to receive either alendronate 10 mg po qd or placebo. Outcome variables included BMD determined by dual-energy x-ray absorptiometry, bone-specific alkaline phosphatase as a marker of bone formation, N-telopeptide as a marker of bone resorption, and adverse events were assessed before and at six and 12 months. At 12 months, the increase in the lumbar spine was 3.6% for combination therapy vs. 1.0% for HRT alone ($P < 0.001$). At the trochanter (hip), it was 2.7% vs. 0.5% ($P < 0.001$). The most commonly used estrogen preparations were conjugated equine estrogens (75%), micronized estradiol (10%), and transdermal estradiol (8%). Patients responded similarly to treatments regardless of age and duration of previous HRT. Overall, the incidence of side effects and adverse events was similar in both groups. In particular, the incidence of drug-related gastrointestinal side effects was identical in both groups. There were no hip or symptomatic vertebral fractures in either group during the study.

COMMENT BY SARAH L. BERGA, MD

The previous dictum regarding the concomitant use of a bisphosphonate and HRT was that, since both were antiresorptives, no additional gain in bone mineral density was to be expected from the use of both.

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Further, there was the concern that concomitant use might oversuppress osteoclastic function (the cells that resorb), thereby severely depressing osteoblastic function, resulting in too steep of a decrease in bone turnover. Since bone turnover, in addition to density, is important to skeletal structural integrity, too little is undesirable. This study suggests that, contrary to expectations, the use of both alendronate and standard doses of HRT increased bone density at both the spine and the hip trochanter. Two small studies that used etidronate found similar results, but this study is the only one that used a prospective, randomized design with such a large population of postmenopausal women.

Based on this study, one can be reasonably confident in recommending the use of both therapies in women with established osteoporosis or osteopenia. I envision the following as the most parsimonious approach for most women. Initiate HRT as the first line of defense in women with low bone mass because of the multiple other associated salutary benefits. One of these benefits is maintenance of mental speed of processing, an attribute implicated in the pathogenesis of falls. Then, if bone density does not increase or declines, add a bisphosphonate. Of course, to know whom to treat demands that one know the bone density.

It is preferable to know BMD before initiating HRT, so that the response to it can be gauged. A woman on a low dose of estrogen would also have the option of increasing the estrogen dose, regardless of whether a bisphosphonate is begun, if the skeletal response to the initial dose of HRT was insufficient. In the past, the clinical recommendation was to choose between HRT and bisphosphonates. An either/or approach is no longer dictated. For instance, women with severe osteoporosis might want to start both concomitantly, if they are not already on HRT. The population in this study involved women with a mean duration of HRT use of 10 years. All had a bone density at hip or spine of less than 2.0 SD and had already had a fracture.

While the group treated with both HRT and alendronate showed somewhat greater gains in BMD, it is important to note that even women on long-term HRT continued to accrue some BMD while in the HRT arm. I think most practitioners believe that HRT will stabilize BMD. Certainly, that is an appropriate goal in someone with adequate BMD, but women with a history of fracture and severe osteopenia and osteoporosis benefit from a more ambitious treatment goal. Rather than relying on increasing the estrogen dose in those taking HRT, one now also has the option of adding a bisphosphonate. (*Dr. Berga is Associate Professor, Departments of Obstetrics, Gynecology, Reproductive Sciences, and Psychiatry, University of Pittsburgh.*) ❖

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An Infectious Etiology of CAD? Cytomegalovirus in the Pathogenesis of Atherosclerosis

ABSTRACT & COMMENTARY

Synopsis: *Susceptibility to the atherogenic effects of CMD depends, at least in part, on the capacity of the host to suppress CMV-induced inflammatory activity.*

Source: Zhu J, et al. *J Am Coll Cardiol* 1999;34:1738-1743.

Zhu and associates have long been interested in the possible infectious etiology of atherosclero-

sis. In this study, cytomegalovirus (CMV) infection was assessed in 238 subjects undergoing evaluation of chest pain with invasive testing. Any angiographic evidence of atherosclerosis classified a patient into the coronary artery disease (CAD) group. CAD risk factors were carefully assessed. Anti-CMV IgG antibodies and CRP were assayed. Of the entire cohort, two-thirds had evidence of CAD on angiography, ranging from plaquing to angiographic stenoses. Multivariate analysis indicated that CAD was associated with advanced age, male gender, and hypercholesterolemia; Zhu et al believe that their cohort represents typical CAD patients. CMV levels were found to be strongly correlated with CAD, with mean values significantly higher in these individuals compared to those without CAD (0.89 vs 0.68 mg/dL; P = 0.01). Elevated CRP remained a significant predictor of CAD after adjustment for traditional CAD risk factors (OR 2.4; P = 0.02). Furthermore, of the two-thirds of the patients who had positive anti-CMV IgG antibodies, mean CRP was 0.88 vs. 0.69 mg/dL in those who were seronegative (P = 0.02). After adjusting for other risk factors, Zhu et al conclude that "CMV infection is an independent determinant of CRP levels."

Nevertheless, while 70% of the CAD group had antibodies to CMV, 54% of the non-CAD group were also CMV seropositive. Thus, while elevated CRP was associated with CAD, CMV seropositivity did not achieve statistical significance. With increasing seropositivity and/or elevated CRP levels, the prevalence of CAD was greater. Thus, the highest rates (78%) were noted when both were elevated, and only 22% of individuals without CAD were CMV seropositive with an elevated CRP. Zhu et al hypothesize that CMV stimulates an inflammatory response in the host, which induces a variable reaction, and that the magnitude of the inflammatory response will influence the development of or progression of CAD. They conclude that CMV is an independent determinant of elevated CRP and "predisposes to the induction of chronic subclinical inflammation." Thus, variation of the inflammatory response may be an important factor in determining whether an individual who has been exposed to CMV progresses to atherogenesis. Zhu et al believe that this helps explain the conflicting observations in the literature regarding the relationship of CMV to CAD. These results are compatible with the hypothesis that susceptibility to the atherogenic effects of CMD depends, at least in part, on the capacity of the host to suppress CMV-induced inflammatory activity. (*Dr. Crawford is Robert S. Flinn Professor, Chief of Cardiology, University of New Mexico, Albuquerque.*) ❖

Using the Berlin Questionnaire to Identify Patients at Risk for Sleep Apnea Syndrome

ABSTRACT & COMMENTARY

Synopsis: *This study attempted to use a survey as a means of identifying patients with sleep apnea in the primary care setting. The survey addressed the presence and frequency of snoring behavior, waketime sleepiness or fatigue, and history of obesity and hypertension. Patients were classified as high risk for sleep apnea if two of these three findings were present. The survey was followed by a portable unattended sleep study in a subset of patients to measure respiratory disturbance index (RDI). Approximately 37% of the respondents were found to be in the high-risk category as defined by the survey. Risk grouping was useful in prediction of the RDI. Netzer et al conclude that the Berlin questionnaire is useful in identifying patients who are likely to have sleep apnea.*

Source: Netzer NC, et al. *Ann Intern Med* 1999;131:485-491.

The obstructive sleep apnea-hypopnea syndrome is a common disorder found in 2-4% of the general population.[1] This syndrome is characterized by excessive daytime sleepiness, disruptive snoring, repeated episodes of upper airway obstruction during sleep, and nocturnal hypoxemia. However, recognition of the syndrome by community physicians is low. Only 7% of women and 12% of men who had moderate to severe illness reported receiving a diagnosis of sleep apnea from a medical encounter in Wisconsin.[2] Specialist intervention, physician education, or simply asking patients to report their symptoms has been found useful in identifying patients at risk.

The Berlin questionnaire consists of a series of questions selected from the literature that attempt to predict the presence of sleep disordered breathing. The questions focus on snoring, daytime sleepiness, blood pressure, and obesity. The patients were classified in high- and low-risk groups based on responses in three different categories. High risk was defined as persistent symptomatic snoring (> 3-4 times/wk) in category 1, in category 2 by persistent waketime sleepiness, drowsy driving, or both (> 3-4 times/wk) and in category 3, by a history of high blood pressure or a body mass index (BMI) more than 30 kg/m^2. High risk of having sleep apnea was defined by being

high risk in at least two different categories.

The survey was conducted at five primary care sites in Cleveland, Ohio. Each patient visiting these sites was given a questionnaire to complete. Of 1008 surveys, 744 (74%) were entered for analysis. A portable sleep study was completed for 100 patients and their RDI and oxygen saturation were recorded. A blinded independent researcher performed the scoring.

Approximately 52% reported snoring, of which 24.6% felt that their snoring was louder than normal speech. Forty-eight percent reported snoring at least 3-4 times per week and 55% said their snoring bothered others. Sixteen percent reported breathing pauses during sleep at least once per month. Thirty-four percent felt not rested after a full night's sleep 3-4 times per week and 39% experienced waketime tiredness or fatigue 3-4 times per week. Nineteen percent said that they had fallen asleep while driving, of which 4% said they did it at least 3-4 times per week.

Approximately 44% of men and 33% of women were found to be at high risk. High-risk group patients were more likely to have a higher BMI, to be male, to have a history of high blood pressure, to have gained weight recently, to snore loudly, to have observed apneas, to be tired during waketime, and to fall asleep at the wheel. Approximately 13% of the respondents underwent a sleep study. The high-risk group had a mean respiratory disturbance index (RDI) of 21.1 ± 18.5, oxygen desaturation index of 19.4 ± 19.5, and lowest SaO_2 of 82.6% ± 9.2%. The values in the low-risk group were RDI of 4.7 ± 7.7, oxygen desaturation index of 5.9 ± 7.6, and lowest SaO_2 of 89.9% ± 5.9%. Eighty-six percent of the patients with an RDI of higher than 5 were identified using the survey. The patients at low risk had a higher likelihood of having an RDI of lower than 5. Qualification in only one symptom category did not predict RDI threshold as well as grouping did (85% vs 63-78%).

COMMENT BY DAVID OST, MD

Despite being common, the majority of primary care physicians are unaware and have no easy means to diagnose the Apnea Hypopnea syndrome. The prevalence of this disorder is estimated to be as high as 2-4%.[1] Stoohs and colleagues estimated that as many as 20% of the primary care patient population might have sleep disordered breathing.[5] Because most patients with sleep disorders are referred to a tertiary care center for diagnosis and treatment, many patients remain undiagnosed because of lack of resources and infrastructure. The Walla Walla project attempted to educate physicians and the public in order to provide the necessary equipment and technical expertise necessary for sleep disorder diagnosis and treatment.[3] Ball and colleagues found that in the vast majority of cases, sleep apnea remains undiagnosed. Community physicians were capable of discovering and caring for such patients when resources were provided. Haponik and colleagues also demonstrated that physicians uncommonly obtained sleep histories, while physicians trained in sleep were more likely to ask about sleep.[4] They concluded that major changes in physician attitude and behaviors are essential in order to recognize sleep problems.

Netzer and colleagues used a survey and established its role reasonably well in the diagnosis of sleep apnea in this study. It has a high sensitivity of 86% in identifying patients with an RDI of higher than 5. The major advantage of this technique is that it identifies the high-risk patient without personal physician encounters or referring the patient to a tertiary care center. Due to ease and convenience of the technique, physicians and patients could participate in this process alike. However, despite the advantages of the test, Netzer et al cautioned that apart from its validation in different primary care settings, physician judgment is still needed to initiate a management system, to detect unusual cases, and to recognize causes for waketime sleepiness other than sleep apnea. ❖

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Name-Based Reporting for HIV

ABSTRACT & COMMENTARY

Source: Osmond DH, et al. *Ann Intern Med* 1999;131: 775-779.

This interesting survey challenges the concept that name-based surveillance of HIV infection will result in improved partner notification and more timely access to health care for infected contacts. The Multistate Evaluation of Surveillance for HIV Study Group surveyed 1913 people with AIDS who tested positive for HIV in five states with name-based surveillance. Surprisingly, just as many sexual and needle contacts were notified by HIV-infected persons who were tested anonymously as those identified through the con-

fidential testing sites and tracked through the health department (3.85 vs 3.80 partners). Furthermore, both types of contacts sought medical care with a similar frequency and within a similar time-frame. In general, about two-thirds of infected contacts began medical care within two months irrespective of the means of notification. About 6% of patients had not sought medical care within three years of receiving a positive HIV test.

Most patients who delayed seeking care indicated that they either felt well or were not yet ready to deal with their HIV. Other common reasons for delaying care was uncertainty about where to go and concerns regarding the affordability of care.

COMMENT BY CAROL KEMPER, MD

Only 8.6% of patients expressed concern that they would be identified to the health department. Contrary to current thought, named-based surveillance reporting for HIV may not increase identification of infected contacts nor does it appear to facilitate their access to medical care. Improved counseling at anonymous test sites with better information about health care options is needed. (*Dr. Kemper is Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases, Santa Clara Valley Medical Center.*) ❖

Pharmacology Update

Dofetilide—Tikosyn

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

In october, the fda approved a new anti-arrhythmic drug for the maintenance of, and conversion to, normal sinus rhythm in patients with highly symptomatic atrial fibrillation/atrial flutter. Dofetilide, marketed as Tikosyn by Pfizer, is a Vaughan Williams Class III antiarrhythmic agent that prolongs action, potential duration, and the effective refractory period.

Indications

Dofetilide is indicated for the maintenance of normal sinus rhythm in patients with atrial fibrillation/atrial flutter of longer than one week duration who have been converted to normal sinus rhythm. It is also indicated for the conversion of atrial fibrillation and atrial flutter to normal rhythm. Due to the potential for life threatening ventricular arrhythmias it should be reserved for patients in whom atrial fibrillation/atrial flutter is highly symptomatic.

Dosage

The dose must be individualized according to calculated creatinine clearance and QTc. The usual dose is 500 mcg twice daily. Prior to the administration of the first dose, the QTc must be determined using an average of 5-10 beats. The drug is contraindicated if the QTc is greater than 440 msec or 500 msec in patients with ventricular conduction abnormalities. If the heart rate is less than 60 beats per minute, QT interval should be used. Use in patients with more than 50 beats per minute has not been studied. The QTc should be monitored 2-3 hours after the first dose and adjusted for QTc prolongation and monitored after each subsequent dose for a minimum of three days.[1] This requires initiation of the drug in a monitored inpatient setting.

Dofetilide is available as 125 mcg, 250 mcg, and 500 mcg capsules.

Potential Advantages

Results from pooled data of randomized trials in patients with supraventricular arrhythmias (n = 2023) indicated that treatment with dofetilide does not adversely affect survival compared to placebo (hazard ratio 1.1, 95% CI 0.3-4.3).[2] In patients with congestive heart failure and left ventricular dysfunction (n = 1518), dofetilide, compared to placebo, reduced the risk of hospitalization for worsening heart failure (odds ratio 0.75, 95% CI, 0.63-0.89).[3] Patients with atrial fibrillation (AF) at baseline (n = 391) had a higher overall rate of conversion at 12 months (44% vs 13%; $P < 0.001$) and were less likely to have recurrence (hazard ratio 0.35, 95% CI 0.22-0.57). In sinus rhythm at baseline, fewer patients developed atrial fibrillation (2% vs 6.6%; $P < 0.001$). Dofetilide does not appear to adversely affect survival in patients with heart failure with or without a recent MI, or AF at study entry.[1,3]

Potential Disadvantages

Dofetilide does not appear to reduce mortality. It prolongs QT interval in a dose-dependent manner and can cause serious ventricular arrhythmias (i.e., torsades de points).[1] In the supraventricular tachycardia study population, the incidence of torsades de pointes was 0.8% while in the heart failure population it was 3.3%.[1,2] The majority, 76%, of these episodes have been reported to occur within the first three days of therapy.[3] Dofetilide should be initiated in the hospital with three days of cardiac monitoring. The concomitant use of dofetilide and other drugs that can prolong the QT interval should be avoided. These include macrolides, cisapride, tricyclic antidepressants, and phenothiazines. Cimetidine has been reported to increase dofetilide plasma levels by 58%.[1]

Comments

Dofetilide is a selective inhibitor of the rapid component of the delayed rectifier potassium current, which results in prolongation of the action potential duration and the effective refractory period. It does not affect repolarizing potassium channels, sodium channels, adrenergic alpha-receptors, or beta receptors.[1,4] The drug does not affect AV node conductance, sinus node function, or cardiac output. In patients with chronic atrial fibrillation and/or atrial flutter, dofetilide had a conversion rate of about 30% at a dose of 500 mcg twice daily and an estimated probability of 58-66% of remaining in normal sinus rhythm for 12 months.[1] In the two survival studies, the Danish Investigations of Arrhythmia and Mortality on Dofetilide (DIAMOND), dofetilide did not appear to increase the risk of mortality in patients with structural heart disease.[1,3] Dofetilide can cause torsade de pointes and the dose must be carefully initiated and titrated based on creatinine clearance and QTc. Therapy should be initiated in the hospital or an equivalent setting with appropriate EKG monitoring. Pfizer is developing a comprehensive educational program for health care professionals on the required in-hospital initiation of therapy and the use of the dosing algorithm. Their marketing suggests that the drug will only be available to physicians and hospitals that have participated in the educational program.

Dofetilide costs $3.60 per day for 250 mcg or 500 mcg taken twice daily.

Clinical Implications

AF is the most common form of cardiac arrhythmia. Its incidence increases with age and is associated with cardiovascular disorders such as coronary heart disease, valvular heart disease, or cardiomyopathy.[5] Management of AF is generally divided between conversion and maintenance of sinus rhythm or control of ventricular rate and prevention of thromboembolic events. Management strategies depend on the clinical presentation and the patient's need for restoration and maintenance of sinus rhythm.[5] Antiarrhythmics have been used to convert as well as to maintain sinus rhythm, but their effect on survival has generally not been favorable, especially in patients with heart failure or post-myocardial infarction. Post-MI patients treated for premature ventricular beats with encainide, flecainide, or moricizine have increased risk of mortality compared to placebo in the Cardiac Arrhythmia Suppression Trials (CAST, CAST II).[6,7] D-sotalol and class I antiarrhythmics have been shown to increase mortality compared to placebo in patients with AF and heart failure in the Stroke Prevention in Atrial Fibrillation trial (SPAF) and the Survival with Oral D-Sotalol trial (SWORD).[8,9] Amiodarone, on the other hand, may have neutral or slightly improved mortality.[10] In the Heart Failure Survival Trial of Antiarrhythmic Therapy (CHF-STAT), amiodarone showed improved survival in patients who converted to sinus rhythm compared to those who did not convert.[11] Amiodarone has not been approved by the FDA for the management of AF. Dofetilide appears to be neutral with regard to mortality and, thus, is an option for patients with AF and heart failure. Implantable cardioverter defibrillators may be another treatment option in the future. ❖

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CME Questions

9. Coronary atherosclerosis may be associated with:
a. herpes simplex.
b. cytomegalovirus.
c. HIV.
d. All of the above

10. The prevalence of the Sleep Apnea-Hypopnea syndrome is estimated to be:
a. 1-2%.
b. 2-4%.
c. 4-6%.
d. 6-8%.

11. Which of the following is *not* true about dofetilide?
a. It is a beta blocker.
b. It should be started only in a monitored setting.
c. It prolongs QT intervals.
d. It is not associated with adverse survival compared with placebo.

12. In postmenopausal women with low bone density on hormone therapy, the addition of alendronate leads to further increases in bone density.
a. True
b. False

By Louis Kuritzky, MD

Effects of Influenza Vaccination of Health Care Workers on Mortality of Elderly People in Long-Term Care: A Randomized Controlled Trial

Most of the excess mortality from influenza occurs in persons older than 65 years of age. Even though vaccination of senior citizens, especially in long-term care facilities, does reduce mortal complications of influenza, incomplete vaccination rates and poor immune response result in spotty coverage of this at-risk population. Influenza in health care workers, as manifest by seroconversion, occurs in as many as 23% of hospital staff, and may be a source of transmission of influenza virus to seniors. A pilot study in which health care worker vaccination was evaluated demonstrated a 41% reduction in elderly mortality from influenza, prompting this more definitive trial.

Twenty U.K. hospitals participated in this trial—only half of which offered immunization to their health care workers (n = 1217). Randomized patients were also equally divided among the 10 hospitals that used influenza immunization and 10 that did not (n = 1437).

Only 50% of health care workers accepted the offered influenza immunization. Nonetheless, the senior mortality in the immunization-offered health care worker sites was 42% lower than in the nonimmunized sites. Although, for inexplicable reasons, the background immunization level of the elderly patients in the immunization-offered sites was slightly higher than the other sites, this variance is insufficient to account for the mortality benefits seen as a result of health care worker immunization. ❖

Carman WF, et al. Lancet 2000; 355:93-97.

Hyperinsulinemia, Hyperglycemia, and Impaired Hemostasis

Only about half of the increased risk for cardiovascular mortality observed in patients with diabetes is accounted for by traditional risk factors. Insulin resistance (IR) and hyperinsulinemia (HI) have been suggested as factors to which additional cardiovascular morbidity and mortality are attributable. The mechanism(s) by which IR and HI negatively affect cardiovascular health remain to some degree speculative, but a role in modulation of coagulation status has been suggested. Meigs and colleagues evaluated a subgroup (n = 1331) of the Framingham Study population to test the hypothesis that altered glucose tolerance and insulin resistance would be associated with increased hemostatic factor levels, independent of other factors like obesity and lipids.

Hypercoagulability has been associated with increased levels of fibrinogen, factor VII, and von Willebrand factor; decreased fibrinolytic potential has been associated with increased plasminogen activator inhibitor 1 (PAI-1) antigen, or tissue-type plasminogen activator (tPA) antigen.

In this study, fasting hyperinsulinemia was associated with increased levels of PAI-1 antigen, tPA antigen, factor VII antigen, von Willebrand factor antigen, fibrinogen, and blood viscosity. Additionally, it has been suggested that elevated levels of PAI-1 predispose to low-stability plaque formation. Meigs et al comment that the atherogenic effects of glucose and insulin abnormalities seen in diabetes may be mediated through aberrations in hemostatic factors. ❖

Meigs JB, et al. JAMA 2000;283: 221-228.

Primary Care Outcomes in Patients Treated by Nurse Practitioners or Physicians

Assessment of outcomes for patients seen by different providers has been hampered by differences in practice patterns, populations, and responsibilities of clinicians in different settings. This study draws from a New York clinical setting staffed by nurse practitioners in some sites and physicians in others, where 24-hour ambulatory care is provided by both providers to a population predominantly of Hispanic origin (Dominican Republic). The work responsibilities, including opportunity for consultation, referral, and hospitalization, were the same. Patients with asthma, diabetes, and hypertension were selected for audit, since they were felt to represent a cohort in which outcomes might be reliably monitored (n = 1316 enrolled).

Overall patient satisfaction was the same for both groups. Overall health status improved over the duration of the study and was equal for both groups. Asthma and diabetic control was equal for both groups, but nurse practitioner care achieved significantly better diastolic blood pressure control than physicians. No differences were found in health care service utilization between providers. Though statistically significant, a clinically insignificant difference in patient ratings of technical skill, personal manner, and time spent was found in favor of physicians. These data suggest that nurse practitioner and physician outcomes in primary care settings are equivalent. ❖

Mundinger MO, et al. JAMA 2000; 283:59-68.

Any Marriages in the Tachycardia?

By Ken Grauer, MD

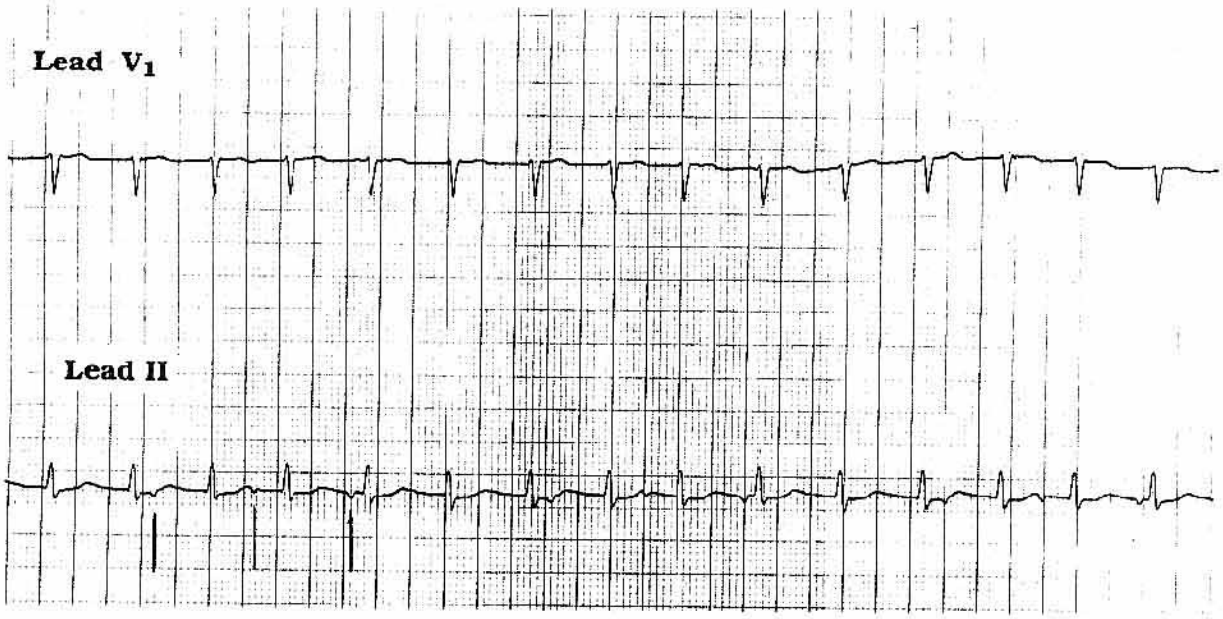

Figure. Post-operative telemetry tracing from a patient with severe valvular heart disease.

Clinical Scenario: The telemetry tracing shown in the Figure was obtained from an acutely ill 49-year-old man who had just returned to the intensive care unit following valvular heart surgery. How would you interpret the rhythm in this tracing? What are the three most common causes of this rhythm disturbance?

Interpretation: This is a difficult tracing to interpret. However, use of a deductive approach greatly facilitates arriving at the correct answer. The five key parameters for rhythm interpretation are assessing for P waves (the presence and nature of atrial activity); determining QRS width (distinction when possible between ventricular and supraventricular rhythms); calculating heart rate; determining regularity; and when P waves are present, assessing for a relationship ("marriage") between P waves and QRS complexes (to determine if P waves are conducting). The memory aid, "*Watch your P's and Q's—and the three R's*," facilitates recall of these five key parameters. The rhythm in the Figure is clearly supraventricular (as determined by the fact that the QRS complex is narrow). The rate is rapid and the rhythm almost (but *not* completely) regular. Atrial activity is present—however, the PR interval continually changes, suggesting AV dissociation. Putting together these findings results in an interpretation of junctional tachycardia (at a rate of about 125/minute) with AV dissociation. The most common causes of accelerated junctional rhythm or junctional tachycardia are digitalis toxicity, inferior infarction, and post-operative state, especially when the patient has undergone cardiovascular surgery.

A subtle additional point about this rhythm revealed by close inspection (measured with calipers) is slight variation in the R-R interval. Despite this, the *atrial* rhythm remains regular throughout the rhythm strip (use calipers to verify this, beginning with the 3 short vertical lines). It is likely that the slightly early occurring beats in this tracing (the 4th, 9th, and 14th QRS complexes) are "capture" beats being conducted by P waves that occur during a non-refractory portion of the cardiac cycle. ❖

In Future Issues:

Classic Teaching About Intussusception in Adults Needs Revision