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# FAMILY PRACTICE ALERT™

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## MVP Revisited

ABSTRACTS & COMMENTARY

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

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

Mitral valve prolapse (mvp) is believed to be a common disorder that may cause symptoms and lead to valve replacement. However, the true prevalence of MVP in the community setting has not been established since two-dimensional echocardiographic criteria were refined. Thus, Freed and colleagues evaluated the two-dimensional echocardiograms in 3736 unselected subjects participating in the Framingham Offspring Study. Technically inadequate echoes excluded 245 (7%). MVP was analyzed in the parasternal and apical long axis views, and superior displacement of the leaflets greater than 2 mm and at least a 5-mm-thick leaflet were required to diagnose classic MVP. Nonclassic MVP was diagnosed when leaflet thickness was less than 5 mm. MVP was found in 84 subjects (2%): 47 with classic and 37 with nonclassic (1% each). Complications in the MVP patients included syncope in three, atrial fibrillation in one, stroke in one, one had endocarditis, and one had mitral valve replacement. These incidences of the complications were similar to those without MVP.

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

## INSIDE

A higher prevalence of MVP has been reported in young patients with cerebrovascular events, but the true prevalence with modern two-dimensional echocardiographic criteria is unknown. Thus, Gilon and associates used a case-controlled design to evaluate 213 patients 45 years old or younger with ischemic stroke or transient ischemic attacks (TIA) by echocardiography and compared them to 263 controls. Cardiac or vascular causes of the cerebral ischemic event were identified in 142 of the 213 patients; 93 had major vessel disease in the neck and 49 had a cardiac source of embolism. Of the 71 without overt cardiovascular disease, only 16 had no risk factors for cerebral ischemic events. MVP was found in four of the 213 cerebral event cases (2%) and seven of the 263 controls (3%). Interestingly, none of the patients in either group had classic MVP, more than trace MR, or left atrial enlargement. The frequency in the 71 patients without identifiable cardiovascular disease was 3% and none of the 16 without any risk factors for cerebral ischemic events had MVP. Gilon et al conclude that MVP defined by new, more specific, echocardiographic criteria is not more common among young individuals with cerebral ischemic events as compared to controls.

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## COMMENT BY MICHAEL H. CRAWFORD, MD

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

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

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

Not surprisingly, the physical examination was not very effective at detecting MVP since it is well known that most cases of mild mitral regurgitation are not detectable

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

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

# Vaccination for *Haemophilus Influenzae* Type b is not Associated with a Risk of Diabetes Mellitus

ABSTRACT & COMMENTARY

***Synopsis:*** *Based on new studies, it appears unlikely that H. influenzae type b vaccination or its timing causes type 1 diabetes mellitus in children.*

**Source:** Karvonen M, et al. *BMJ* 1999;318:1169-1172.

Because most children receive various vaccines on many occasions during their first five years of life, it is not at all surprising that a variety of conditions and events may occur in proximity to a childhood immunization. A question in most of these cases of vaccination-disease associations is whether the vaccine actually was causally related to the condition or was only coincidental. There have been a number of linkages of childhood immunizations and specific diseases that have led to public concern (recently an alleged relationship between hepatitis B immunizations and multiple sclerosis prompted a moratorium on HpB immunizations in France). Damage to the pancreatic beta cells leading to type 1 diabetes is believed to be caused by environmental factors including infections and possibly immunizations.

In 1988, the vaccine for *H. influenzae* type b was given to virtually all children born in Finland as part of a nation efficacy trial. The design of the trial was that children born between 1985 and 1987 who were born on odd-numbered days received the conjugate Hib vaccine at 3, 4, and 6 months of age followed by a booster at 14-18 months of age. Children born on even-numbered days were a control group and received Hib vaccine at 24 months of age only. Of interest is the fact that Finland has the highest incidence of type 1 diabetes mellitus in children younger than 14 years of age in the world, and its incidence has been increasing by 2-3% per year since the 1940s. Classen and Classen described an apparent accelerated increase in the incidence of type 1 diabetes in children after the national program for Hib immunization began in 1988 and have speculated that there may be a causal association.[1,2] However, because of the near universality of immunizations in infancy and childhood and the relative rarity of diabetes, an enormous database of appropriate data is necessary to generate statistically convincing conclusions.

Karvonen and associates from the Diabetes and Genetic Epidemiological Unit of the National Public Health Institute in Helsinki compared the cumulative incidence and risk of type 1 diabetes in three cohorts of Finnish children: those born 24 months before the start of the national Hib immunization program was begun; those in the 1988 trial cohort who received Hib vaccine at 3 months of age followed by a later booster; and the control cohort from the trial who were vaccinated at 24 months only. The data were obtained from a nationwide hospital discharge registry. There were no differences between the incidence of type 1 diabetes in the three groups. Karvonen et al conclude that it is unlikely that *H. influenzae* type b vaccination or its timing causes type 1 diabetes mellitus in children.

### COMMENT BY HOWARD PEARSON, MD, FAAP

It is hoped that similar rigorous analysis will be used to establish or disprove causal relationships between beneficial procedures such as childhood immunizations

and rare pediatric conditions. In fact, a recent article showed no association between autism and MMR immunizations.[3] (*Dr. Pearson is Professor of Pediatrics, Yale University School of Medicine.*) ❖


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# Low-Dose Oral and Vaginal Misoprostol for Cervical Ripening and Labor Induction

ABSTRACT & COMMENTARY


***Synopsis:*** *A 50-mcg dose of oral misoprostol is somewhat less effective than a 25-mcg dose of intravaginal misoprostol given every four hours for cervical ripening.*



**Source:** Wing DA, et al. *Am J Obstet Gynecol* 1999;180: 1155-1160.


Many physicians are interested in oral misoprostol for cervical ripening and the induction of labor. Wing and colleagues from the University of Southern California randomized 220 women with medical or obstetric indications for labor induction to either 50 mcg of oral misoprostol or 25 mcg of intravaginal misoprostol every four hours. At enrollment, all subjects had a Bishop score less than 5. After 24 hours, the misoprostol was stopped. Those women with a Bishop score more than 7 began induction of labor with oxytocin. When subjects began active labor, they received routine intrapartum management, including oxytocin augmentation if needed, without regard to treatment group. The primary outcome measure was successful labor induction, defined here as vaginal delivery occurring within 24 hours after that start of induction.

Of the orally treated women, 30.9% had successful labor inductions, compared with 47.3% of vaginally treated women, a statistically significant difference (P = 0.01). The oral treatment group required a mean of 29.6 hours to deliver, while the vaginal treatment group required 25.4 hours (P = 0.03). The oral misoprostol group required a mean of 3.3 doses, the vaginal group 2.3 doses (P < 0.0001). Approximately 75.4% of the oral group required oxytocin, compared with 59.1% of the vaginal misoprostol group (P = 0.01). There were no significant differences in rates of uterine tachysystole, hyperstimulation, chorioamnionitis, neonatal outcomes, or cesarean deliveries between the two groups.

## COMMENT BY ELIZABETH MORRISON, MD, MSEd

Misoprostol is an effective, safe, and inexpensive choice for cervical ripening and labor induction. Oral administration will allow outpatient cervical ripening, an attractive and cost-saving option for patients, physicians, and health systems. Recent research has focused on determining the best dose for oral misoprostol.

Oral misoprostol fans will be somewhat disappointed with the results of the study by Wing et al. For all outcome measures, low-dose oral misoprostol was significantly less effective than intravaginal misoprostol for ripening the cervix and inducing labor, although both the oral and vaginal doses appeared quite safe, and both allowed labor induction within a mean of 30 hours.

Several points should be taken into account when interpreting the results of this study. Subjects included women with varying gestational ages, less than 10% of the subjects were postdates. Women with hypertension and diabetes mellitus made up one-quarter of the study population, and their concomitant medical problems might have caused them to react differently to the misoprostol. Since the study medications were discontinued after 24 hours, it was not possible to determine whether the oral misoprostol might have had a stronger effect if given less frequently but, as other studies are exploring, for a longer treatment period.

These caveats aside, the study by Wing et al continues to support the idea that a 50-mcg oral misoprostol dose may be less effective than one would desire for cervical ripening at or near term. The answer may ultimately lie in using a higher dose of oral misoprostol with a less frequent dosing interval. Other investigators have found that a 100-mcg dose of oral misoprostol is as safe and effective as the same dose given intravaginally.[1] Oral doses of200 mcg have also been studied,[2] but tend to cause unacceptably high rates of uterine hyperstimulation.

It will be fascinating to see the results of ongoing and future studies of 100-mcg, 50-mcg, and even 25-mcg oral doses of misoprostol for cervical ripening. We also need to know how various oral misoprostol doses compare with placebo. When these issues are resolved, many of us hope to be able to offer appropriately-selected women the option of oral misoprostol for cervical ripening and labor induction. Although Wing et al did not find a 50-mcg dose given every four hours to be as effective as they had

hoped, another dosing regimen may be found that is more effective in future studies. (*Dr. Morrison is Director of Maternity Care Education, Assistant Clinical Professor of Family Medicine, University of California, Irvine.*) ❖


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*Pharmacology Update*

# Orlistat Capsules (XenicalRoche Laboratories)

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

The fda has approved the highly anticipated lipase inhibitor, orlistat (Xenical-Roche) for the management of obesity. The drug is an inhibitor of pancreatic and gastric lipases in the lumen of the gastrointestinal (GI) tract. Inhibition of these enzymes results in a reduction of the amount of dietary fat absorbed and associated caloric intake. Roche has already marketed orlistat in 17 countries, where it has been used in more than 1 million patients.

**Indications**

Orlistat is indicated for obesity management (weight loss and weight maintenance) when used in conjunction with a reduced-calorie diet. It is indicated for obese patients with an initial body mass of 30 kg/m$^2$ or greater and in patients with an initial weight of 27 kg/m$^2$ or greater in the presence of other risk factors such as hypertension, diabetes, or dyslipidemia.[1]

**Dosage**

The recommended dose of orlistat is 120 mg three times a day with fat-containing meals. It may be taken during or up to one hour after meals.[1] Gastrointestinal side effects may be reduced by consuming a high-fiber diet and reducing the amount of dietary fat.[8]

Patients should be advised to take a multivitamin supplement containing fat-soluble vitamins. These should be taken two hours before or after orlistat (e.g., bedtime). Orlistat is available as 120 mg capsules.

**Potential Advantages**

Orlistat acts within the gastrointestinal tract with negligible systemic exposure or systemic effects.[2-4] In clinical trials, orlistat was reported to improve lipid profiles (total cholesterol and low-density lipoprotein cholesterol) and fasting serum insulin.[5] Some studies report an improvement in triglyceride levels as well.[6,7] Improved glycemic control has been reported in type 2 diabetic patients as reflected in glycosylated hemoglobin and reduced sulfonyurea dose compared to placebo.[6]

**Potential Disadvantages**

The most common side effects of orlistat are gastrointestinal and include flatus with discharge (40.1%), oily spotting (32.7%), fecal urgency (29.7%), fatty/oily stool (19.8%), fecal incontinence (11.8%), and increase in defecation (11.1%).[5] Diets high in fat may increase GI side effects. Most GI events last less than one week and generally no more than four weeks. In some individuals, however, GI side effects may continue for more than six months.[1] The absorption of fat-soluble vitamins may be reduced by orlistat, particularly vitamins D, E, and beta carotene. Patients should be advised to take multivitamin supplements containing fat-soluble vitamins while on the drug.[1] Vitamin K absorption may also be decreased. Patients on concomitant warfarin therapy should be monitored carefully.[1] Orlistat should be used in caution with patients with a history of hyperoxaluria or calcium oxalate nephrolithiasis as increased levels of urinary oxalate may result.[1] It is also possible that orlistat may increase gallstone formation since cholecystokinin release is inhibited by the drug, decreasing gallbladder contraction.[11] Orlistat is contraindicated in patients with chronic malabsorption syndrome or cholestasis.[1]

**Comments**

Orlistat is a reverse inhibitor of gastric and pancreatic lipases. Inhibited lipases fail to hydrolyze dietary triglycerides into absorbable free fatty acids and monoglycerides, preventing absorption. Effects are seen as soon as 24-48 hours after dosing. After discontinuation of the drug, fecal fat content returns to pretreatment levels within 48-72 hours.[1] About 30% of ingested fat is lost in the feces during orlistat therapy. Increasing the dose or increasing the amount of dietary fat does not significantly affect the percent of fecal fat lost.[2] In two large trials (n = 892, 688) using intent-to-treat analysis and last observation carried forward technique, orlistat-treated patients lost 8.76 kg-10.3 kg vs. 5.81-6.1 kg for placebo-treated patients at one year when used in conjunction with a hypocaloric diet.[5,9] When subjects were switched to a eucaloric (maintenance) diet after one year of therapy, orlistat-treated patients regained less of their weight lost

(35.2%), compared to 63.4% for placebo-treated patients.[5] Over two years, 34.1% of orlistat-treated patients lost 10% of initial body weight and 57.7% lost 5%, compared to 17.5% and 37.4% for placebo. Weight loss from initial body weight was 7.6% vs. 4.5%. The two-year completion rate ranged from 45% to 63% for these studies. In a one-year study involving obese patients with type 2 diabetes, orlistat reduced total cholesterol, LDL-cholesterol, triglycerides, and improved glycemic control as indicated by decrease in glycosylated hemoglobin (mean, -0.28% vs +0.18%) and significant reduction in the dose of sulfonylurea medication (23% vs 9%).[6] The improvement in the lipid profile appears to be independent of weight lost.[5] Obese patients on orlistat were reported to be less likely to progress from normal glucose tolerance to diabetic or impaired glucose tolerance.[1] The cost of orlistat is about $1.10 per capsule or $3.30 per day.

**Clinical Implications**

Clinically significant obesity is classified as BMI of 30 kg/m$^2$ or greater. The recent National Health and Nutritional Examination Survey III (NHANES III) estimated the prevalence of obesity in the U.S. population to be 22.5%.[10] Current treatment modalities include diet and behavior modification, exercise, pharmacologic intervention, and surgery. Pharmacologic interventions include anorexiants such as phentermine and subutramine. Orlistat offers an antiobesity drug that is different from anorexiants in that it has a nonsystemic mechanism of action. However, the long-term effects of reducing free fatty acids and increasing triglycerides in the GI tract are not known. Weight losses produced by orlistat are quite modest. The weight loss differential between orlistat and placebo is only 3-4% of body weight after one year. The improvements in the lipid profile are also modest (e.g., approximately an 8% reduction in LDL-C), and these changes were only achieved in conjunction with a hypocaloric diet and behavior modification in a controlled study setting. The results may be further clouded by a high dropout rate and potential bias using the last observation carried forward technique for data analysis.[12] It is unclear how the drug will perform in the "real world" setting where diet and lifestyle are less likely to be controlled. ❖

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## CME Questions

**10. The incidence of echocardiographic mitral valve prolapse in the Framingham Offspring Study is:**

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

**11. True statements concerning type I diabetes in children include all of the following *except*:**

a. Its incidence in Finland is the highest in the world.
b. Environmental factors, including infections, have been suggested as a possible etiology.
c. An association with immunization with Hib vaccine has been proven.
d. A causal association with immunizations is difficult to establish.

**12. In the study of oral vs. vaginal misoprostol for "cervical ripening" and labor induction by Wing et al, significant differences between the oral and vaginal treatment groups were found for which one of the following outcomes?**

a Uterine hyperstimulation
b. Neonatal Apgar scores
c. Rates of cesarean delivery
d. Rates of labor induction within 24 hours

**13. Which is true about orlistat?**

a. It suppresses appetite.
b. It prevents carbohydrate absorption.
c. Most people lose about 30% of their body weight.
d. Very little of the drug is absorbed systemically.

*By Louis Kuritzky, MD*

## Fexofenadine HCL on Quality of Life and Work, Classroom, and Daily Activity

Second generation antihistamines (2-GA) have been developed to avoid the adversities common to first generation agents (1-GA), such as sedation, drowsiness, and performance impairment. Since these 2-GA have little ability to cross the blood-brain barrier and are less lipophilic, they should be relatively free of the common 1-GA side effects. Multiple trials have demonstrated that these agents are safe and efficacious for seasonal allergic rhinitis. The current study was designed to measure the effect of fexofenadine, a 2-GA, on general health, disease-specific quality of life, and work, classroom, and daily activity impairment. Tools used for measurement of outcomes included the Rhinoconjunctivitis Quality of Life Questionnaire, the Allergy-Specific Work Productivity and Activity Impairment Questionnaire, and the SF-36.

Almost 2000 patients participated in two randomized, placebo-controlled trials that were pooled for final analysis. At baseline, substantial numbers of individuals suffered embarrassment by allergy symptoms some to all of the time (70%), and being troubled by practical problems such as having to carry tissues or rub/blow their nose repeatedly (98%); also, more than 91% of sufferers reported impairment in ability to do daily activities, work productivity, and classroom productivity.

Within one week of active treatment, patients reported significantly improved quality-of-life scores and work performance. Classroom performance and missed time from class were similarly improved with fexofenadine 60 mg bid as soon as one week into active treatment. In addition to overt symptom control, fexofenadine is effective in enhancing important life quality and performance issues for seasonal allergic rhinitis sufferers. ❖

*Tanner LA, et al. Am J Managed Care 1999;5(4):S235-S247.*

## Egg Consumption and Risk of Heart Disease

Common wisdom has suggested that reduction in egg consumption may be beneficial for cholesterol lowering and, hence, reduced risk of cardiovascular end points. Though widespread in its intuitive appeal, there are few data to support such an intervention. This report used two ongoing prospective cohort studies—the Health Professional Follow-up Study (1986-1994) and the Nurses Health Study (1980-1984)—to assess the relationship of egg consumption and cardiovascular end points. Combined, the population of 117,933 men and women provides more than 1000 cardiovascular end points from which to derive associations.

There was no evident increased risk for any cardiovascular end point associated with egg consumption. This lack of increased risk was true whether subjects consumed less than one egg, 2-4 eggs, 5-6 eggs, or more than eight eggs per week.

In subgroup analysis, diabetic men and women had an increased risk of CHD when they consumed more than one egg per week (RR = 1.49-2.02). The observation that diabetic men and women demonstrated modest increased risk should stimulate further evaluation in this population in particular; postulates as to the diabetic-egg-CHD relationship include aberrancies in cholesterol transport from decreased apolipoprotein E and increased apolipoprotein C-III levels in diabetic patients.

Ho and associates conclude that egg consumption as high as 1 egg daily or greater is not associated with an increased risk of cardiovascular end points. ❖

*Ho FB, et al. JAMA 1999;281:1387-1394.*

## Fasting Plasma Glucose and Glycosylated Hemoglobin

The diagnoses of diabetes mellitus (DM) has important health and social implications. Recent revision of diagnostic criteria for DM suggests that persons with fasting plasma glucose 126 mg/dL or greater be diagnosed as diabetic, whereas previously the diagnostic cutoff had been 140 mg/dL. The current study evaluated whether persons with DM diagnosed by the new criteria manifest abnormal hemoglobin A-1-C levels, the diagnostic marker by which treatment is indicated and monitored.

Davidson and colleagues had data on hand from two large data sets, the National Health and Nutrition Examination Survey (NHANES III) (n = 2284), and the Meta-Analysis Research Group Data Set (MRGDS) (n = 7908), from which they were able to compare impaired fasting plasma glucose levels with hemoglobin A-1-C levels.

Less than 0.2% of persons from NHANES III with fasting plasma glucose over 126 had a hemoglobin A-1-C greater than 7.1%, the generally acknowledged demarcation level indicating necessity for treatment. Similarly, less than 2.5% of MRGDS of subjects had a hemoglobin A-1-C greater than 7.3% when fasting plasma glucose was greater than 126.

Davidson et al suggest that improved accuracy of the diagnosis of diabetes could be achieved by restricting the diagnosis to those with elevated fasting plasma glucose coupled with abnormal hemoglobin A-1-C greater than 7.7, and that individuals with less impairment of hemoglobin A-1-C should be classified as having impaired fasting glucose, treated with diet and exercise alone. ❖

*Davidson MB, et al. JAMA 1999;281: 1203-1210.*

# ECG with an Echocardiographic Diagnosis

*By Ken Grauer, MD*

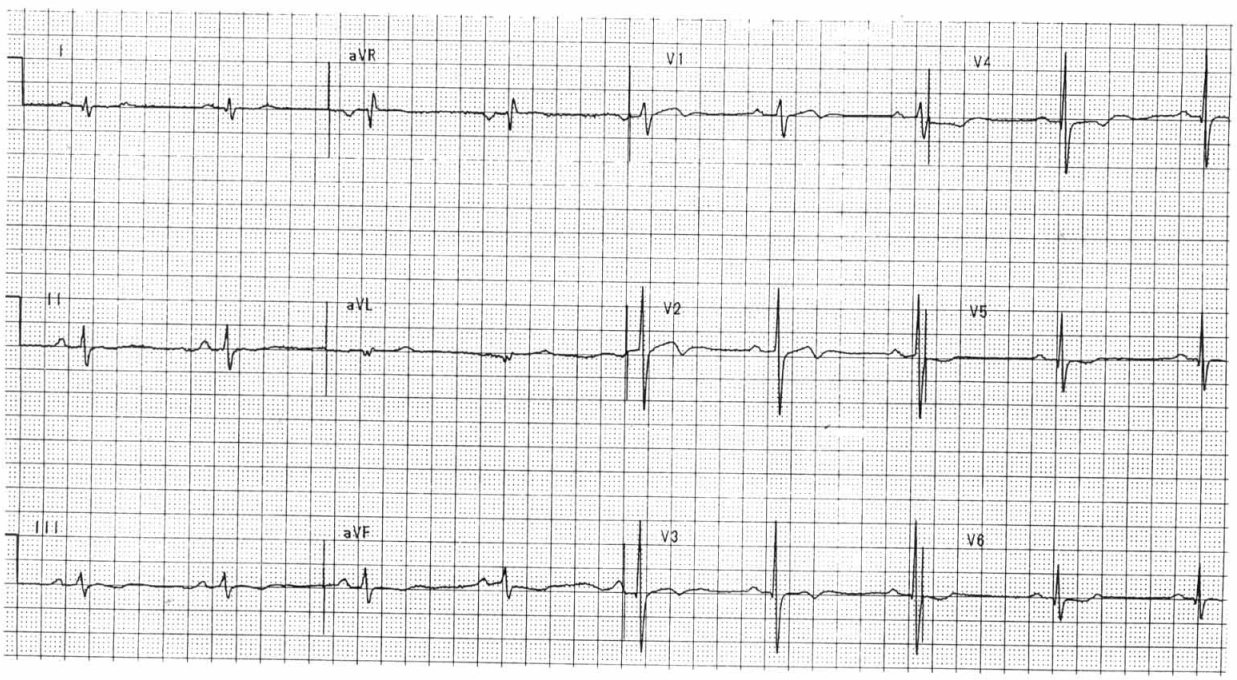


**Figure.** ECG obtained from a 56-year-old man with increasing fatigue.

**Clinical Scenario.** The ECG shown in the Figure was obtained from a previously healthy 56-year-old man with a history of gradually progressive fatigue. No chest pain. No history of prior infarction. The patient has never smoked. An echocardiogram was diagnostic and distinctly abnormal. Can you guess what the echo might show?

**Interpretation.** The rhythm is sinus bradycardia at a rate of 50 beats/minute. All intervals are normal. The mean QRS axis is indeterminate (QRS complexes are nearly equiphasic in all six limb leads). There is no ECG evidence of chamber enlargement. In the precordia leads transition occurs early; small q waves are seen in leads I, aVL, and $V_3$ through $V_6$; and there is nonspecific ST segment flattening with shallow T wave inversion in leads $V_2$ to $V_4$.

The overall ECG picture is nonspecific in nature. However, in view of the hints provided in the history (the patient was previously healthy, he does not smoke, and has no history of prior infarction)—the early transition with relatively prominent R waves in anterior precordial leads suggests prominent septal forces. The patient had nonobstructive hypertrophic cardiomyopathy with septal hypertrophy that was disproportionately enlarged compared to left ventricular wall thickness (asymmetric septal hypertrophy or ASH). It is likely that the small narrow q waves in leads $V_3$ through $V_6$ are also the reflection of prominent septal forces. Although the ECG will usually be abnormal in patients with hypertrophic cardiomyopathy, the changes seen are most often nonspecific and nondiagnostic. This would have been the case here had there not been the hints we have given. ❖

**In Future Issues:** **Does Aspirin Attenuate the Beneficial Effects of ACE Inhibitors?**