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Maybe We Should Put Statins in the Water

ABSTRACT & COMMENTARY

Synopsis: *Statins are associated with a 22% relative risk reduction in the risk of deep venous thrombosis in people 65 and older; further, they are associated with a decreased risk of deep venous thrombosis in women receiving hormone replacement therapy.*

Source: Ray JG, et al. *Arch Intern Med*. 2001;161:1405-1410.

This paper is actually 2 retrospective analyses of large cohorts of individuals at risk for deep venous thrombosis (DVT). In the first analysis, they calculated the hazard ratio for new DVT development in 125,862 Ontarians who were free of documented atherosclerosis, venous thromboembolism, or cancer in the prior 3 years. The mean age of participants was 72.9 years, and the observation period was 1.4 years. Of these patients, 77,993 were statin users and had a hazard ratio of 0.78 (CI, 0.69-0.87) for new DVT development compared with those who used thyroid replacement therapy. These findings were controlled for age, gender, prior hospitalization, new cancer, and treatment with aspirin, coumadin, or estrogen. Those individuals who used nonstatin lipid-lowering agents did not show a similar reduction in DVT risk. In the second analysis of 89,508 women, Ray and colleagues found that those women who were taking estrogen replacement therapy (n = 29,165) were at increased risk for DVT (hazard ratio, 1.16; CI, 1.01-1.33) compared with those who were not. Statins appeared to lower that risk (hazard ratio 0.68; CI 0.59-0.79) compared with those receiving thyroid replacement therapy. This reduction was not seen with nonstatin lipid-lowering agents.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) are in widespread use to prevent cardiovascular disease in people with elevated lipid levels. Ray et al undertook the current study because the Heart Estrogen Replacement Study (HERS) suggested a 50% risk reduction of venous thromboembolism in women who used statins.[1] Because the HERS study was not designed to evaluate this effect of statins, further specific investigation of their effects on DVT development is warranted.

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INSIDE

This study is an important step in that direction.

Ray et al make several interesting observations in their discussion. First, the rate of spontaneous discontinuation of lipid-lowering medications by patients is very high; at least half of patients stop taking these meds within a year of the initial prescription, most within the first 3 months.[2,3] This may not be true in Ontario, where, as Ray et al proudly proclaim, "The Ontario Health Insurance Plan covers all medical care and prescription drug costs for every Ontario Senior Citizen." Second, the rate of DVT development in older women on estrogen replacement therapy may be much higher than previously recognized. In this study, the rate of DVT and pulmonary embolism in women on estrogen was 12.6 per 1000 person years, twice that seen in the HERS study.[1] Ray et al point out that the women in the HERS study were younger and were more likely to be on aspirin or lipid-lowering agents because they were known to have coronary heart disease. For me, the take home messages are to lower the threshold to prescribe statins, particularly in women on estrogen replacement therapy, and to regularly encourage their use. ❖

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Internal Medicine Alert, ISSN 0195-315X, is published twice monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

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GST Registration Number: R128870672.

Periodical postage paid at Atlanta, GA.

POSTMASTER: Send address changes to ***Internal Medicine Alert***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $18. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

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Subscription Prices

United States
$269 per year (Student/Resident rate: $110).

Multiple Copies
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Does Pravastatin Prevent the Development of Diabetes Mellitus?

ABSTRACT & COMMENTARY

Synopsis: *Pravastatin therapy resulted in a 30% reduction in the hazard of developing DM.*

Source: Freeman DJ, et al. *Circulation.* 2001;103:357-362.

Most previous investigations into the relationship of pravastatin and glucose tolerance had been equivocal and have yielded inconclusive results.[2-3] The West of Scotland Coronary Prevention Study (WOSCOPS) database, however, has now provided us with sufficient information to prospectively determine the effects of pravastatin therapy on the risk of developing diabetes mellitus (DM) in a specific population with follow-up data ranging from 3.5 to 6.1 years.[1] Freeman and colleagues evaluated the effects of pravastatin therapy and the risk of developing DM in a total of 5974 men aged 45-64 years. During this study 139 subjects became diabetic and it was determined that, in this population, pravastatin therapy resulted in a 30% reduction in the hazard of developing DM.

COMMENT BY HAROLD L. KARPMAN, MD, FACC, FACP

Freeman et al have determined that pravastatin was effective in preventing the onset of DM with a *P* value of 0.42 in the WOSCOPS cohort consisting of 5974 men. It should be noted that such therapy was effective on a long-term basis and that the subjects had, on average, normal triglyceride levels at baseline. The mechanism by which pravastatin reduces a subject's risk of developing DM is not clear, howev-

er, the beneficial effects of pravastatin therapy on glucose-intolerant subjects had previously been shown in the CARE trial in which significant reductions in cardiovascular risks occurred in the pravastatin-treated subjects.[4]

Three known effects of pravastatin therapy may have played a primary role either individually or collectively in preventing the development of DM in the WOSCOPS subjects. Pravastatin therapy reduced triglycerides by an average of 12%, and since it has been known for many years that elevated triglyceride levels are associated with the development of DM,[5] it is quite possible that a treatment effect mediated through a change in plasma triglyceride levels may have prevented the onset of glucose intolerance in these subjects. However, it should be noted that other lipid-lowering drugs do not appear to improve insulin resistance suggesting that triglyceride lowering in itself probably does not explain the observed effect.[6] Second, pravastatin has been demonstrated to have anti-inflammatory effects and it has been postulated that the drug may interrupt the natural progression from central obesity to insulin resistance by reducing cytokine production which may be responsible for the metabolic syndrome associated with insulin resistance. Finally, improvement in endothial function seen in patients on pravastatin therapy has been shown to result in diminished capillary recruitment which may significantly influence selective tissue perfusion and thereby benefit glucose and insulin transport.[7]

Regardless of the exact mechanisms involved, it would appear that pravastatin therapy may have reduced the propensity of the subjects within the WOSCOPS to develop DM; this effect may have been one of the important mechanisms which contributed significantly to the observed positive cardiovascular benefits of the drug. The forthcoming results of the Prospective Study of Pravastatin in the Elderly Risk (PROSPER) trial will attempt to prospectively determine if pravastatin truly reduces the risk of developing DM in an elderly population.[7] ❖

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Long-term Outcome of Medical and Surgical Therapies for GERD

ABSTRACT & COMMENTARY

Synopsis: *Surgical therapy is not appropriately recommended as a means of averting future medical therapy or as a preventive measure against esophageal adenocarcinoma.*

Source: Spechler SJ, et al. *JAMA*. 2001;285:2331-2338.

This article provides follow-up on a large cohort of medically and surgically treated gastroesophageal reflux disease (GERD) patients in the VA system for more than 10 years. Of the original patients, 239 (97%) were found. A total of 92% of medical patients (n = 83) and 62% of surgical patients (n = 23) still required regular antireflux medicines. Survival was actually decreased in the surgical vs. medical group, apparently due to cardiovascular deaths. Barrett's esophagus was associated with an annual cancer risk of 0.4% in both medical and surgical patients. One concludes that surgical therapy is not appropriately recommended as a means of averting future medical therapy or as a preventive measure against esophageal adenocarcinoma.

COMMENT BY MALCOLM ROBINSON, MD, FACP, FACG

GERD is extremely common, often presenting to a wide range of physicians. Between 20% and 40% of Americans may have significant GERD symptoms. More ominously, presumably GERD-related esophageal adenocarcinoma has nearly quadrupled in the past 2 decades. There has been considerable controversy regarding the proper role of surgery (such as open or laparoscopic fundoplication) in management of chronic GERD. Some surgeons have suggested that surgery might be an alternative to expensive long-term medical management and that surgery might lessen the risk of subsequent esophageal adenocarcinoma. This VA study provides useful data to refute both of these assertions, and similar results have also been seen in an ongoing European study. For most GERD patients, chronic medical management continues to be the treatment of choice. Needless to say, enthusiastic boosters of new endoscopic techniques for GERD management with the so-called Stretta procedure or endoscopic suturing have no long-term data and such approaches cannot be recommended on other than an investigational basis. ❖

Combined Bisphosphonate and Hormone Treatment

ABSTRACT & COMMENTARY

Synopsis: *Estrogen combined with risedronate increased BMD slightly more than estrogen alone.*

Source: Harris ST, et al. *J Clin Endocrinol Metab.* 2001;86: 1890-1897.

Harris and colleagues report the results of a multicenter, 1-year, double-blind, placebo-controlled study of the effect on bone mineral density (BMD) of risedronate (5 mg daily) combined with conjugated estrogens (0.625 mg daily) compared with estrogen alone in a total of 524 women. Forty-eight percent of the patients also received medroxyprogesterone (5 mg) in a sequential regimen. At the end of 1 year, both treatment groups increased BMD. (*See Table*).

The only differences that achieved statistical significance were those in the femoral neck and midshaft radius. Bone biopsies in a subset of patients demonstrated normal bone structure and mineralization in both groups. After 1 year, there were 4 new vertebral fractures (2.6%) in the hormone-only group and 3 (1.8%) with the combined treatment; however, this study had insufficient power to detect meaningful differences in fractures.

Table

Gain in BMD with Treatment

	Lumbar spine	Femoral neck	Midshaft Radius
Hormone therapy alone	4.6%	1.8%	0.4%
Combined risedronate & hormone therapy	5.2%	2.7%	0.7%

COMMENT BY LEON SPEROFF, MD

There is growing recognition that not all postmenopausal women respond to treatments aimed at the prevention of bone loss. Clinicians have rapidly assumed that the solution is to combine treatments. There are 2 important questions:

1. Will a slightly better gain in bone density mean better protection against fractures?
2. Will a poor responder to 1 treatment respond to an alternative treatment?

Adding alendronate or risedronate to postmenopausal hormone therapy produces a gain in bone density that is about 1-2% greater than with single treatment, indicating that each works through a different mechanism. There is no doubt that both lack of bone loss and a gain in BMD correlate with a reduction in fractures. However, that does not mean that a 7% gain protects against fractures better than a 5% gain. One piece of evidence that suggests a difference in bone density is not the whole story is the fact that raloxifene produces a smaller increase in vertebral bone density compared with estrogen and alendronate, yet the 3 agents are associated with essentially identical reductions in vertebral fractures. No study, thus far, has had a sufficient number of patients followed long enough to provide reliable fracture information with combined therapy compared to single agent treatment.

The percentage of postmenopausal women who respond poorly to single agent treatment varies from 5-20% in various studies. This is a substantial number, and underscores the recommendation to screen 65-year-old women with bone density measurements even if they are on osteoporosis prevention treatment. This would detect the poor responders and provide the opportunity for intervention. However, studies of this group of women have yet to appear in the literature. At this time we can only provide the proper intervention, follow the patient, and learn from the patients.

Recommended Evaluation and Intervention for Poor Responders:

1. Rule out other causes of osteoporosis.
2. Make sure calcium and vitamin D supplementation is adequate.
3. Make sure compliance with the treatment is appropriate.
4. Add another antiresorptive agent to the treatment regimen.
5. After 2 years, assess bone density response.

The bone world has expressed concern that combining 2 agents that both inhibit bone resorption might over time interfere with the dynamics of bone remodeling and ultimately yield more fragile bone. This is speculation at the present time, and the biopsy results in this study indicating normal bone morphology and mineralization are reassuring. This has also been reported with combined alendronate and estrogen treatment.[1] In addition, tetracycline labeling appeared in the biopsy specimens indicating that the necessary bone turnover to repair microdamage was taking place.

At the present time, it is premature to assume that combined agent therapy will yield better fracture protection. We need evidence from bigger studies with longer follow-up. ❖

Dr. Speroff is Professor of Obstetrics and Gynecology, Oregon Health Sciences University, Portland, Ore.

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Brief Report

Carpal Tunnel Syndrome

Sources: Padua L, et al. *Neurology.* 2001;56:1459-1466; Wong SM, et al. *Neurology.* 2001;56:1565-1567; Stevens JC, et al. *Neurology.* 2001;56:1568-1570.

First described by pierre marie and charles foix in 1913, carpal tunnel syndrome (CTS) is the most common abnormality seen in electromyography laboratories across the United States.[1] Multiple treatment modalities exist, including steroids, orally or by injection, the latter first reported by Phalen and Kendrick in 1957.[2] How well do they compare?

Among 60 CTS patients prospectively enrolled, 30 were randomized to local injection of 15 mg methylprednisolone acetate vs. placebo, and 30 to oral prednisolone 25 mg daily for 10 days vs. placebo. Both active treatment groups significantly improved their global symptom score (GSS) at 2 and 8 weeks, but only steroid injection showed significant GSS improvement at 12 weeks.[3] No significant side effects were seen in either group. Steroids work, and a single local injection is better than an oral 10-day course.

Is CTS associated with computer use? Certainly, if you ask many litigation lawyers. However, among 257 of 314 employees identified as frequent computer users who participated in a survey, 181 (70%) reported no CTS symptomatology. Of the remaining 76, 70 were interviewed. Twenty-seven were classified as CTS, 18 possible, and 9 definite. Overall, 10.5% met clinical criteria for CTS which was confirmed by nerve conduction studies in 3.5%. These percentages are comparable to those of the general population. Will this ease the dockets? Wish that it were so!

Lastly, under "why did this merit publication as a full article, and with CME credit to boot," we learn that CTS improves spontaneously. Among 274 hands with idiopathic CTS, spontaneous resolution was associated, surprisingly, with more severe initial symptomatology, as well as younger age, and short duration of symptoms. Milder initial impairment, bilateral baseline symptoms, and positive Phalen sign predicted a poor prognosis. The findings are interesting but this report will not change treatment practices for CTS as they present to your office. It will be a boon to disability lawyers and their clients. A letter to the editor would have sufficed. ❖

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

Pharmacology Update

Twinrix—A New Vaccine for Hepatitis A and B

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

The fda recently approved a vaccine that provides dual protection against hepatitis A and B. Marketed as Twinrix by GlaxoSmithKline Pharmaceuticals, the vaccine combines inactivated hepatitis A vaccine with hepatitis B recombinant vaccine, the antigenic components in Havrix and Engerix B, respectively. The combination reduces the number of injections needed to immunize patients to both viruses from 5 to 3. An exact release date is expected soon.

Indications

Twinrix is indicated for the active immunization of adults (18 years of age or older) against disease caused by hepatitis A virus and infections by all known subtypes of hepatitis B virus.[1]

Dosage

The primary immunization for adults is 1 mL given intramuscularly in 3 doses at 0, 1, and 6 months. The injection should be given in the deltoid region, not in the gluteal region. Administration in the gluteal region may result in a suboptimal response.[1] Each 1 mL dose of Twinrix contains 720 ELISA units (EL.U) of inactivated hepatitis A virus and 20 mcg of recombinant hepatitis B surface antigen (HbsAg).

Potential Advantages

The combined vaccine offers more convenience and potentially better compliance. Twinrix requires 3 injections and 3 sites compared to 5 injections and 5 injection sites (2 for hepatitis A and 3 for hepatitis B).

Potential Disadvantages

Safety and effectiveness of Twinrix have not been established in pediatric patients. The effectiveness in patients age 65 years and older has also not been established.[1]

Comments

The immunogenicity and safety of Twinrix has been demonstrated in more than 1500 subjects. After the completion of the 3-dose regimen, seroconversion was detected in more than 98% of subjects against both hepatitis A and B.[1,2] In a comparative trial, Twinrix was at least as effective as Havrix and Engerix-B administered separately.[1] The antibody titers achieved with Twinrix were actually higher than that achieved with Havrix. This may be attributed to a difference in dosing. Twinrix is given as 3 doses of 720 EL.U at 0, 1, and 6 months while Havrix is given as 2 doses of 1440 EL.U at 0 and 6 months.

The most frequent reported side effects are local soreness and headache or fatigue. These were similar to that reported with Havrix or Engerix-B.[1]

Clinical Implications

Hepatitis B is a viral infection with serious consequences including acute hepatic necrosis, chronic active hepatitis, and cirrhosis of the liver. Chronic hepatitis B infection has been linked to hepatocellular carcinoma. The main modes of transmission are parenteral drug abuse, unprotected sex, visits to high-prevalence countries, exposure to infected body fluids, and high-risk occupations or settings. The CDC estimates that there are 1-1.25 million chronic carriers of hepatitis B in the United States. These persons can infect others in the community. Currently, vaccination is routine in children. This strategy will not only protect persons from infection but reduce disease incidence by reducing transmission.

Hepatitis A is one of the most frequently reported vaccine preventable diseases and is considered a major public health problem.[3] The main mode of transmission is fecal-oral. Contaminated food or water or infected food handlers are a major source of transmission. Unlike hepatitis B, there is no routine childhood vaccination for hepatitis A. Twinrix offers a vaccine for adults who have not been vaccinated with either hepatitis A or B, and is recommended for those at risk of exposure to these viruses. These include travelers to endemic areas (who often are immunized against hepatitis A but rarely against hepatitis B), those with chronic liver disease, high-risk workers (laboratory, sanitation workers, medical personnel), employees of day-care centers, correctional facilities, persons with at-risk behavior (homosexuals, parenteral drug users), military personnel, persons with clotting-factor disease (eg, hemophiliacs), and those in close contact with individuals with hepatitis A.

Twinrix provides a convenient vaccine for the immunization against preventable diseases caused by hepatitis A and B in adults. The duration of protection is at least 4 years.[1] ❖

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CME Questions

8. Statins:

a. have no effect on the development of DVT.
b. reduce the development of DVT to the same degree as do non-statin lipid-lowering agents.
c. reduce the risk of DVT in men, but not in women.
d. reduce the risk of DVT in both men and women, and reduce the rate of development of DVT related to estrogen therapy.
e. have no measurable effect of development of DVT, but appear to be associated with reduced risk of pulmonary embolism, especially in men.

9. Surgical therapy for GERD offers which of the following results as defined by the recently reported VA cooperative study?

a. Surgery affords significant protection against later development of adenocarcinoma in GERD patients.
b. Long-term surgical results include a significantly improved mortality rate as compared to medical management.
c. Surgery patients rarely, if ever, require medical therapy for management of recurrent postoperative GERD symptoms.
d. Surgical intervention for GERD provides unexpected protection from excess cardiovascular mortality in these patients.
e. None of the above

10. The following statements are true regarding osteoporosis prevention therapy *except*:

a. Bisphosphonate and estrogen treatment produce comparable effects on bone density.
b. It is worthwhile to try to gain as much bone density as possible.
c. All the currently approved agents for the prevention of osteoporosis produce comparable effects on reduction of vertebral fractures.
d. There is concern that long-term follow-up of treated patients will yield different results than short-term bone density studies.

11. Which is *not* true about Twinrix?

a. It is less effective than both vaccines given individually
b. It is not approved for children
c. It requires 3 injections
d. It is given at 0, 1, and 6 months

By Louis Kuritzky, MD

Microalbuminuria as a Marker of Preclinical Diastolic Dysfunction in Never-Treated Essential Hypertensives

Normal urinary albumin excretion does not exceed 30 mg/24 h. Microalbuminuria (MAU), defined as 30-300 mg/24 h albumin excretion, is seen in hypertensive and diabetic patients and has been shown to reflect, in addition to propensity for decline in renal function, cardiovascular risk. For instance, MAU is associated with greater incidence of left ventricular hypertrophy (LVH) and LV systolic dysfunction (SDF). LV diastolic dysfunction (DDF) is considered one of the earliest detectable myocardial derangements attributed to hypertension, antedating SDF, but studies have not previously been done relating MAU to DDF in never-treated hypertensives.

This study included never-treated hypertensives (n = 87) that were divided into MAU+ (= 30-300 mg/d albuminuria) and MAU- (= normal albumin excretion) categories, and evaluated for DDF. Diastolic function, as measured by peak LV lengthening rate, was found in MAU+ patients 3 times as often as MAU- patients (67.8% vs 22%).

Grandi and colleagues conclude that in addition to the acknowledged association between MAU+ and other cardiovascular risk, MAU+ is associated with impairment of diastolic ventricular function in asymptomatic hypertensive patients. ❖

Grandi AM, et al. Am J Hypertens. 2001;14:644-648.

Smoking Cessation and the Course of Major Depression: A Follow-Up Study

It has been previously noted that persons attending smoking-cessation clinics have a statistically greater frequency of past episodes of depression than nonsmoking comparators. Additionally, previous depression is linked with smoking recidivism.

The issue of new episodes of major depression attendant to smoking cessation efforts has been little examined. Glassman and colleagues examined 100 smokers with a previous history of major depression who participated in a smoking cessation trial for 2 months. Sertraline was the active agent used to assist smoking cessation (placebo controlled). Patients were not taking antidepressant medications during the 6-month observation period after smoking cessation intervention.

Comparing persons who successfully stopped smoking with those who continued to smoke, the frequency of major depression was 5 times as likely among abstinent persons (31% vs 6%). Interestingly, among abstinent smokers, those who had used placebo were twice as likely to suffer subsequent depression than the group who received active pharmacotherapy (43% vs 19%). Glassman et al conclude that smoking cessation is associated with an elevated risk of recurrence of depression; nicotine may have some effect that alters vulnerability to depression. The evenly distributed frequency of depressive episodes throughout the 6 months postcessation observation period argues against a "sertraline halo" effect. ❖

Glassman AH, et al. Lancet. 2001;357: 1929-1932.

Prophylaxis with Single-Dose Doxycycline for the Prevention of Lyme Disease After an *Ixodes Scapularis* Tick Bite

Though lyme disease may be prevented by vaccination, the cost and need for multiple doses are substantial obstacles to implementation, in addition to imperfect protective effects. To test the applicability of using single-dose pharmacotherapy (200 mg doxycycline PO) in persons who have recently suffered a tick bite from *Ixodes scapularis*, Nadelman and colleagues performed a placebo-controlled trial (n = 482) among persons who had removed a tick within 72 hours of attachment. Subjects underwent physical examination, blood cultures, and *Borrelia burgdorferi* antibody tests at baseline, 3 weeks, and 6 weeks.

Erythema migrans was infrequent, but doxycycline did statistically significantly reduce its occurrence (0.4% vs 3.2%). In regard to the primary end point of the trial (development of erythema migrans), the overall efficacy of doxycycline was 87%.

Nadelman et al conclude that when given within 72 hours of a recognized tick bite, a single dose of 200 mg of doxycycline is highly effective in preventing development of Lyme disease. ❖

Nadelman RB, et al. N Engl J Med. 2001;345:79-84.

In Future Issues:

Antibiotic Treatment in Patients with Persistent Symptoms and a History of Lyme Disease

Chest Pain and Lots of P Waves

By Ken Grauer, MD

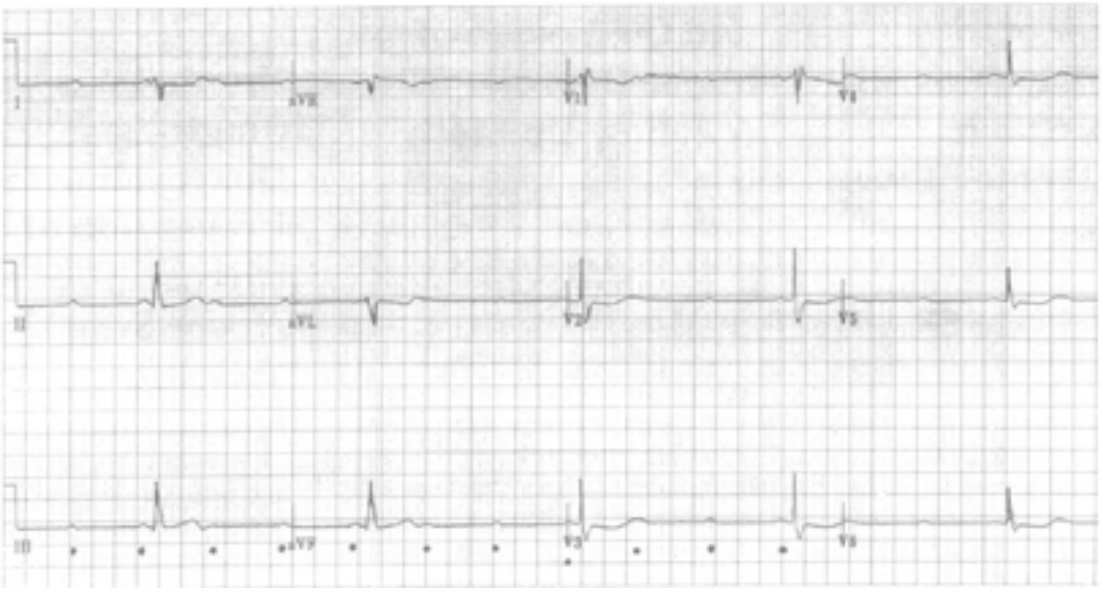

Figure. 12-lead ECG obtained from a 55-year-old woman with chest pain and lots of P waves.

Clinical Scenario: The 12-lead ECG shown in the Figure was obtained from a 55-year-old woman with new-onset chest pain. Many more P waves than QRS complexes are seen on the tracing (*see dots under P waves in leads III, aVF, and V_3*). How would you interpret this ECG?

Interpretation: Although a single lead rhythm strip is lacking, the 12-lead ECG in the Figure can still be interpreted. A narrow-complex marked bradycardia is present that is fairly regular at a rate just over 30 beats/minute. As noted above, many more P waves than QRS complexes are present. The atrial rhythm (marked by the dots) is regular at a rate of between 90-95/minute. Despite the fact that many more P waves than QRS complexes are present, P waves appear to conduct, as evidenced by the presence of a *fixed* PR interval preceding each QRS complex. This finding rules out the possibility of 3° (complete) AV block, in which there is no relationship between P waves and QRS complexes (P waves "march through" the QRS complex when there is 3° AV block). The rhythm must therefore be some type of *high-grade* 2° AV block, in this case with 3:1 AV conduction (3 P waves are present for each QRS complex). Although high-grade AV block (in which many if not most P waves *fail* to conduct) is most often the result of Mobitz II 2° AV block, the *lack* of consecutively conducted P waves anywhere on this tracing precludes definitive diagnosis. It is important to appreciate that on occasion, the usually less severe Mobitz I (Wenckbeach) form of 2° AV block may also be "high grade," with failure of consecutively occurring P waves to conduct. In such situations, the characteristic picture of progressive PR interval lengthening prior to dropping a beat may not be seen.

Analysis of the remainder of the ECG in the Figure reveals marked right axis deviation (RAD) consistent with a left posterior hemiblock (LPHB) pattern, incomplete right bundle branch block (IRBBB) evidenced by an rsr' pattern in lead V_1, early transition (a relatively tall R wave is present in lead V_2), and worrisome ST segment depression in leads I, aVL, and V_2-V_6. An ECG obtained 1 hour earlier showed ST segment elevation in the inferior leads (which has now resolved). The overall picture in this 55-year-old woman with new-onset chest pain is most consistent with acute evolving infero-posterior infarction. Telemetry tracings over the previous hour revealed clear evidence of Mobitz I (Wenckbach) 2° AV block—which in conjunction with the findings of normal QRS duration and acute inferior infarction strongly suggest that the 2° AV block with 3:1 AV conduction seen here is probably also a manifestation of the Mobitz I (Wenckbach) form of 2° AV block. That said—the bifascicular conduction defect and acute infarction with marked bradycardia are clear indication for emergency pacemaker placement. ❖