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Tamoxifen Cuts the Risk of Breast Cancer in Half

ABSTRACT & COMMENTARY

Synopsis: *Despite the risk of thromboembolism, the use of tamoxifen reduces a woman's risk of developing breast cancer by about 50%.*

Source: Fisher B, et al. *J Natl Cancer Inst* 1998;90:1371-1388.

One of the interesting secondary outcomes of the careful clinical studies conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and other multicenter groups through the years has been the observation that women with breast cancer who took adjuvant therapy with tamoxifen not only had a significantly lower rate of disease recurrence but, in addition, had a significantly lower risk of developing cancer in the contralateral breast.[1-4] Because women who have had breast cancer are at high risk of developing a second breast cancer, this secondary benefit from tamoxifen adjuvant therapy led to the notion that perhaps tamoxifen would be capable of influencing the risk of developing breast cancer in other high-risk groups. Tamoxifen has also been shown to have beneficial effects on the risk of cardiovascular disease, the development of osteoporosis, and possibly even the occurrence of dementia and Alzheimer's disease. Balanced against these substantial potential benefits was a small risk of developing estrogen-related complications, such as thromboembolic disease and endometrial cancer, because of the weakly estrogenic effects of tamoxifen.

In light of these considerations, NSABP implemented a randomized clinical trial (NSABP-P1) to examine whether tamoxifen could significantly lower the risk of developing breast cancer in a group of women considered to be at increased risk. Eligibility criteria included the following: age 60 years or older; age 35-59 years with a calculated five-year risk of 1.66% (note that the Breast Cancer Risk Assessment Tool used to calculate the risk [based upon the model of Gail et al[5]] is now available as an interactive computer program through the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER or online at http://cancertrials.nci.nih.gov) or a history of lobular carcinoma in situ; a life expectancy of at least 10 years; a negative breast examination and mammogram within the past six

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months; and no history of thromboembolic disease or deep venous thrombosis. Women with an intact uterus had an endometrial tissue sampling before starting treatment. Primary outcome measures were the rate of development of breast cancer. Secondary outcome measures were the incidence of myocardial infarctions and the incidence of osteoporotic bone fractures.

From April 1992 through May 1997, 13,388 women (of 98,018 undergoing risk assessment) were randomly assigned to receive either tamoxifen 20 mg/d or oral, daily placebo for five years. The trial was a double-blind, placebo-controlled design; 6707 received placebo and 6681 received tamoxifen. Twenty-one percent of women stopped their assigned therapy prematurely—19.7% in the placebo group and 23.7% in the tamoxifen group. Complete follow-up was available on 92.4% of the participants.

In total, 368 invasive and noninvasive breast cancers developed among the 13,175 patients with follow-up, 244 on placebo, 123 on tamoxifen. Of these, 175 cases of those on placebo were invasive and 89 cases on tamoxifen were invasive ($P < 0.00001$ in favor of tamoxifen). The cumulative incidence through 69 months was 43.4 per 1000 women in the placebo group and 22 per 1000 women in the tamoxifen group. Thus, tamoxifen significantly reduced the risk of both invasive and noninvasive breast cancer. Significantly reduced risk was seen in women of all ages: younger than 49, 44% risk reduction (RR); 50-59, 51% RR, and older than 60, 55% RR. Risk was reduced in women with a history of lobular carcinoma in situ (56%) or atypical hyperplasia (86%). Significantly reduced risks were observed in all risk categories.

Tamoxifen-treated patients did not have a reduced risk of myocardial infarction, but this may be related to the length of follow-up. Bone fractures were significantly reduced in the tamoxifen arm. Endometrial cancer occurred with increased incidence on the tamoxifen arm: 36 cases (13/1000 women) vs. 16 cases (5.4/1000 women) on the placebo arm. All the cancers on the tamoxifen arm were FIGO stage I. More women who received tamoxifen developed deep vein thrombosis (35 vs 22) and pulmonary embolus (18 vs 6). The incidence of strokes and cataracts was not significantly different on the two arms.

COMMENT BY DAN LONGO, MD, FACP

Well, it's hard to imagine news much better than this. The use of tamoxifen reduces a woman's risk of developing breast cancer by about 50%. A bonus from the treatment is a reduction in osteoporosis and the morbidity associated with fractures. At this particular time of follow-up, tamoxifen has not yet shown a beneficial effect on deaths from heart disease, but only a small fraction of patients have died so far. This study did not assess cognitive end points, but it is also possible that tamoxifen-treated patients will have less age-related cognitive impairment.

With these documented and not-yet-documented gains come some downside risks. The risks of thromboembolic disease and endometrial cancer are somewhat increased by taking tamoxifen. However, the balance of risk and benefit is overwhelmingly in favor of benefit. The subset of patients with genetic mutations that increase their risk has not yet been examined; however, blood samples are available to determine BRCA1 and BRCA2 phenotypes and such correlations will be made in future analyses. In addition, given the broad efficacy of tamoxifen in diverse risk groups, the question must be asked about how high the risk must be before the risk-benefit ratio is favorable. Modifications of the existing algorithms are currently being made to help with these decisions.

Furthermore, we may not yet have gotten all the benefit that is possible to obtain from tamoxifen use. The question remains open whether longer duration of tamoxifen treatment would exert greater benefits. In addition, it is not yet clear whether the newer selective estrogen receptor modulators (SERMs), such as raloxifene, will have different or greater effects than tamoxifen. Ongoing studies, including NSABP-P2, are addressing this question. The success of this study makes interpretation of other ongoing studies somewhat complicated. In my opinion, it is no longer

Family Practice Alert, ISSN 1093-2534 is published 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 rate postage pending at Atlanta, GA.

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

Back issues: $20. Missing issues with 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

$219 per year (Student/Resident rate: $110).

Multiple Copies

1-9 additional copies: $110 each; 10 or more copies: $63 each.

Outside the United States

$249 per year plus GST (Student/Resident rate: $125 plus GST).

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appropriate to include a placebo arm in breast cancer prevention studies. The new SERMs need to be demonstrated to be superior to tamoxifen rather than placebo. Primary care physicians should develop a level of comfort using the risk assessment tool and applying it to individual patients. If an individual is found to be at increased risk of breast cancer, the first choice would be to enter the patient on a prospective randomized trial. If that is not possible, women should be informed of the risks and benefits of tamoxifen use and be permitted to obtain the benefits proven in this landmark study. (*Dr. Longo is Scientific Director, National Institute on Aging, Baltimore, MD.*) ❖

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Cardiovascular Risk Factors—How Important are They to Control in Diabetic Patients Without Known Coronary Artery Disease?

ABSTRACT & COMMENTARY

Synopsis: *Cardiovascular risk factors should be modified as aggressively in diabetic patients without coronary artery disease as is recommended for nondiabetic (or diabetic) patients with prior myocardial infarctions.*

Source: Haffner SM, et al. *N Engl J Med* 1998;339:229-234.

Patients with proven coronary artery disease have 3-7 times greater mortality than do patients without known coronary artery disease.[1,2] Diabetic patients are particularly at significant risk for developing symptomatic coronary artery disease[3,4] as are patients with elevated serum cholesterol levels,[4,5] whether they are afflicted with diabetes. However, it had not been previously clearly determined whether it is necessary to treat diabetic patients who have not previously suffered myocardial infarctions as aggressively with respect to risk factor modification as is recommended for post-myocardial infarction patients whether they are diabetics.

A report recently published in the *New England Journal of Medicine* from the University of Texas Health Science Center at San Antonio, Texas, and from the Turku University in Finland addressed this question by comparing the seven-year incidence of both fatal and nonfatal myocardial infarctions that occurred in 1373 nondiabetic patients with the incidence in 1059 diabetic subjects.[6] Their data suggested that diabetic patients without previous myocardial infarctions had as high a risk of myocardial infarction as nondiabetic patients with previous myocardial infarctions. They conclude that cardiovascular risk factors should be modified as aggressively in diabetic patients without coronary artery disease as is recommended for nondiabetic (or diabetic) patients with prior myocardial infarctions.

COMMENT BY HAROLD L. KARPMAN, MD

The data in the present study were obtained from a Finnish population-based database, which is a central registry of all patients with diabetes who receive reimbursement for drugs. Although the data are well collected, one potential limitation of the current study is that the mortality rate from coronary artery disease in Finland is among the highest in the world.[6] The seven-year incidence of myocardial infarctions among nondiabetic patients with and without prior myocardial infarction at baseline was 18.1% and 3.5%, respectively, whereas the incidence of myocardial infarction in diabetic patients with and without prior myocardial infarction at baseline was 45% and 20.2%, respectively. Therefore, the incidence rates in nondiabetic patients with prior myocardial infarctions and in diabetics without prior myocardial infarctions are essentially equivalent. Obviously, a prospective study comparing the effects of different levels of lipid-lowering therapy on coronary heart disease in diabetic subjects, with and without previous history of myocardial infarctions, would be a definitive way to demonstrate that the conclusions derived from this population-based study are accurate. However, in the short term, it would appear to be prudent to treat all diabetics (whether they have or have not previously suffered a myocardial infarction) with vigorous risk factor modification in order to reduce the incidence of new and/or recurrent myocardial infarctions. (*Dr. Karpman is Clinical Professor of Medicine, UCLA School of Medicine.*) ❖

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Epididymitis, Testicular Torsion, and Torsion of Appendix Testis

ABSTRACT & COMMENTARY

Synopsis: *In the 38 patients who had a color Doppler ultrasound, the sensitivity was 100% and the specificity was 97% for identifying testicular torsion.*

Source: Kadish HA, Bolte RG. *Pediatrics* 1998;102:73-76.

When a child presents with scrotal pain or swelling, it can be difficult to distinguish the causes. Investigators at the Primary Children's Medical Center in Utah report on a retrospective review of patients younger than 18 years of age with these conditions who recently presented to their hospital. Ninety patients were included—64 with epididymitis, 13 with testicular torsion, and 13 with torsion of appendix testis.

The peak incidence of all three conditions was during ages 9-14 years. Incidence of testicular torsion peaked at 12-16 years. Patients with torsion of appendix testis were evenly distributed between 1-14 years, and patients with epididymitis were seen in all age groups, with a peak incidence of 8-12 years. Historical features, such as fever, nausea, vomiting, dysuria, sexual activity, and history of trauma, were not helpful discriminators. Compared with epididymitis, patients with testicular torsion and torsion of appendix testis were more likely to present within 12 hours of the onset of symptoms. All patients with testicular torsion had an absent cremasteric reflex and a tender testicle, compared, respectively, with 14% and 69% of patients with epididymitis, and 0% and 31% of patients with torsion of appendix testis. The testicular lie was normal in all patients with epididymitis and torsion of appendix testis, yet was normal in only half of the patients with testicular torsion. Ninety-seven percent of patients with epididymitis had a tender epididymis, compared with only 23% of patients with testicular torsion. Only patients with torsion of appendix testis had isolated tenderness at the superior pole of the testis. In the 38 patients who had a color Doppler ultrasound, the sensitivity was 100% and the specificity was 97% for identifying testicular torsion.

COMMENT BY LEONARD FRIEDLAND, MD

There are some take-home messages from this retrospective review. In contrast to the history, the physical examination is very helpful when attempting to distinguish between testicular torsion, epididymitis, and torsion of appendix testis. Think testicular torsion when you note an absent cremasteric reflex, tender testicle, or abnormal testicular lie. Isolated tenderness at the superior pole of the testis is highly characteristic of torsion of appendix testis. Color Doppler ultrasound can be helpful in distinguishing among the causes; however, missed cases of testicular torsion have been reported. The practice at my institution mimics that of Kadish and associates: urology consultation is obtained in all uncertain cases. I was taught that epididymitis was a disease of sexually active patients, yet this paper confirms my experience that it occurs in children as well as adolescents. Epididymitis was observed across all age ranges; only 15% of patients with epididymitis had an abnormal urinalysis, and in those patients none cultured had an STD. Add epididymitis to your differential of the acute scrotum, even in young children. (*Dr. Friedland is Assistant Professor of Pediatrics and Medicine, Temple University School of Medicine and Director of Pediatric Emergency Medicine, Temple University Hospital, Philadelphia, PA.*) ❖

Vitamins A, C, and E in Cancer Therapies

ABSTRACT & COMMENTARY

Synopsis: *Vitamin E and vitamin C supplements are recommended in modest doses, as they are safe and may help prevent some cancers.*

Source: Kaegi E. *Can Med Assoc J* 1998;158:1483.

Because large doses of supplemental vitamin a have serious toxic effects, retinoids like beta carotene (a provitamin—i.e., transformed in vivo into vitamin A) have been touted as treatment for some cancers. There are laboratory and animal data to suggest the increased production and tumoricidal activity of white blood cells and macrophages with retinoids, especially beta carotene and analogues of vitamin A. Clinical data are contradictory, though recent studies suggest an increased incidence of lung cancer with beta carotene supplementation.

Although epidemiologic data suggest a preventive effect of foods rich in vitamin C against stomach and cervical cancer, either through an antioxidant or nitrosamine blocking action, the therapeutic effects of supplemental vitamin C are less clearly documented. Anecdotal reports and uncontrolled case series suggest improved survival, although two randomized controlled

trials of vitamin C therapy with advanced cancer were negative. Safety at up to 1000 mg daily has been repeatedly reported. Proponents believe that megadose, intravenous vitamin C earlier rather than later in illness, has a better chance of having a beneficial clinical effect.

Like vitamin A, vitamin E is fat soluble. It is most commonly ingested in food as d-tocopherol, usually gamma, and as a supplement, most of which is synthetic, or dl-alpha tocopherol. Most clinical trials have been done with dl-alpha tocopherol. Vitamin E's lipid antioxidant and immunostimulatory effects are thought to be responsible for its anticancer effects. Toxicity with high doses—over 800 IU—can include nausea, diarrhea, and blurred vision. High doses may also interfere with the absorption of anticoagulants, iron, and vitamin B12. Oral leukoplakia, a cancer precursor, may be successfully treated with vitamin E, and invasive prostate cancer risk may be reduced with 50 mg (approximately 100 IU) daily.

COMMENT BY JOHN La PUMA, MD

Vitamin E and vitamin C supplements are recommended in modest doses, as they are safe and may help prevent some cancers. Beta carotene supplements may be dangerous and are not recommended. Strong cancer prevention data, especially for gastrointestinal disease, exist for low saturated fat diets that are rich in high fiber, largely unprocessed plant foods. A diet that puts fruits, vegetables, grains, and legumes in the middle of the plate and makes animal foods side dishes is probably the best medicine. Because 250 almonds or hazelnuts are needed for 100 IU of vitamin E daily, however, a supplement is the best way to get this vitamin. (*Dr. La Puma is Director, C.H.E.F. Skills Research, Cooking, Healthy Eating, and Fitness [C.H.E.F.], Alexian Brothers Medical Center, Elk Grove, IL.*) ❖

Pharmacology Update

Leflunomide (Arava)

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

The fda recently approved a new disease modifying agent for the treatment of rheumatoid arthritis (RA), the first new drug to be approved for this indication in more than a decade. Leflunomide (Arava-Hoechst Marion Roussel) was given a priority review by the FDA and was approved with the indication of retarding the structural damage of the disease, the first medication of its kind to receive this indication.

Leflunomide seems to work by causing cell arrest of lymphocytes involved in the autoimmune process. The drug is a de novo uridine synthesis inhibitor. It acts by inhibiting dihydroorotate dehydrogenase and tyrosine kinases, with the former action predominating.[1,6] This action is postulated to arrest stimulated cells at the G1 phase, thereby not allowing the production of ribonucleotides needed to proceed to the S phase.[1] Leflunomide is metabolized to an active metabolite (A77 1726) which has a long elimination half-life of approximately 16 days.

The drug is marketed by Hoechst Marion Roussel and is manufactured in France by Usiphar.

Indications

For the treatment of active rheumatoid arthritis to reduce signs and symptoms and to retard structural damage as evidenced by X-ray erosions and joint space narrowing.[2]

Dosing Information

Leflunomide is supplied as 10-mg, 20-mg, and 100-mg tablets. Due to the long elimination half-life, a loading dose is needed to achieve steady-state concentration more quickly. A loading dose of one 100-mg tablet daily for three days is recommended. A daily dose of 20 mg is recommended as a maintenance dose. If there are problems with tolerance, the dose may be reduced to 10 mg.[2] NSAIDs and low-dose corticosteroids may be used concomitantly with leflunomide.[2]

Should leflunomide need to be discontinued for pregnancy or other reasons, the elimination half-life can be reduced from over 1 week to about 1 day by administering cholestyramine 8 g three times daily for 11 days.[2]

Potential Advantages

Leflunomide provides an alternative to disease-modifying antirheumatic drugs (DMARDs) such as methotrexate or sulfasalazine particularly when the latter agents are not tolerated. Leflunomide does not seem to be associated with (albeit rare) severe and occasionally life-threatening toxicities that are seen with methotrexate such as pulmonary toxicity and myelosuppression. In the European comparative trial two cases of agranulocytosis were reported with sulfasalazine (n = 132) and none in the leflunomide group.[9] Coadministration of folate is not necessary.

Potential Disadvantages

Due to its potential teratogenic effect, leflunomide is contraindicated in women who are or may become pregnant. In addition, men wishing to father a child should consider discontinuing leflunomide.[2] Elevation of liver enzymes (ALT and AST) occurs in 5-10% of patients in clinical trials. Elevations were generally mild (2 x ULN). ALT should be performed at baseline and monitored monthly for several months. If the levels are stable, further levels should be determined by the individual clinical situation.[2] Leflunomide is not recommended in patients with hepatic insufficiency and should be used with caution in patients with renal insufficiency.

It is not recommended in patients with severe immunodeficiency, bone marrow dysplasia, or severe uncontrolled infections; use of live virus vaccines should be avoided during or for a period of time after stopping leflunomide.[2]

Common side effects include diarrhea (17-27%) and rash (10-12%).[2] These side effects appear to be more common than with methotrexate.[2]

Rifampin increases the peak levels of leflunomide by about 40% and caution should be exercised during concomitant therapy.[2] The FDA has requested that Hoechst conduct a drug-interaction study involving cytochrome P450 3A4 inhibitors such as erythromycin or ketoconazole.[3]

Comments

The approval of leflunomide was based on three controlled trials (2 European and 1 US/Canada) involving 1839 patients and treatment durations of up to 52 weeks. Efficacy was assessed by improvement of signs and symptoms and by radiographic assessment of structural damage. Relief of signs and symptoms was determined by using American College of Rheumatology (ACR) 20 Responder Index. A responder is a patient who had 20% improvement in both tender and swollen joint counts and in three of the following five criteria: physician global assessment, patient global assessment, function/disability measure, visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein. Progression of structural damage was assessed radiographically using the Sharp Score, a composite score of erosions and joint space narrowing in hands/wrists and forefeet.[2]

One trial compared leflunomide with placebo and methotrexate, another compared leflunomide with placebo and sulfasalzine, and the third compared methotrexate with leflunomide. Leflunomide was dosed at 20 mg daily following an initial loading dose of 100 mg/day for three days, methotrexate was dosed at 7.5 mg/week increasing to 15 mg/week, and sulfasalazine was dosed at 2 g/day. Results indicate that the efficicacy of leflunomide is similar to methotrexate and sulfasalazine and superior to placebo. One study, however, indicated that methotrexate showed a higher response rate than leflunomide (69% vs. 56%), although there was no significant difference in Sharp Scores.[2] Treatment effect is generally evident by one month and stabilized by 3-6 months.[2] Additional details of one of the phase III trials, in abstract form, suggested that leflunomide-treated patients may achieve sustained response earlier and of longer duration, with greater improvement in quality of life scores compared to methotrexate.[7,8]

Clinical Implications

Rheumatoid arthritis affects about 1% of the general population. Initial pharmacotherapy of rheumatoid arthritis is generally nonsteroidal anti-inflammatory drugs (NSAIDs). Patients in whom disease remains active after adequate treatment with NSAIDs are candidates for DMARD therapy such as methotrexate, sulfasalazine, and hydroxchloroquine.[4] Methotrexate is often selected as the initial DMARD as it is effective and generally well tolerated. Over 50% of patients taking methotrexate continue for three years or longer,[4,5] however GI symptoms, stomatitis, alopecia, and rare, but potentially serious, myelosuppression or pulmonary toxicity have been reported. Leflunomide provides an alternative to methotrexate and other DMARDs. Pulmonary toxicity has not been reported with leflunomide, although GI symptoms such as diarrhea seem to be more frequent. The efficacy of leflunomide in patients not responding to methotrexate or other DMARDs remains to be determined. Rheumatology consultation should be considered before initiating DMARD therapy.

Leflunomide is expensive; the average wholesale cost is $8 per day or about $3000 per year. This is more than twice the cost for methotrexate (15 mg/week, not including the cost of folate) and more than 10 times the cost for sulfasalazine (2 g/d). ❖

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CME Questions

33. Which of the following statements is true regarding women at increased risk of breast cancer?

a. Tamoxifen use daily for 10 years significantly reduces the risk of breast cancer.
b. Tamoxifen use daily for two years significantly reduces the risk of breast cancer.
c. Tamoxifen use daily for five years significantly reduces the risk of breast cancer.
d. The beneficial effects of tamoxifen on breast cancer risk are outweighed by toxicities associated with tamoxifen use.
e. Tamoxifen and raloxifene are equally effective in the prevention of breast cancer.

By Louis Kuritzky, MD

Dietary Sodium Reduction

Dietary sodium restriction is sometimes helpful in management of hypertension, both as a mechanism to lower blood pressure as a sole intervention, and as a method to enhance responsiveness to some antihypertensive medications. On the other hand, adverse impact on glucose metabolism, probably as a consequence of RAA activation attendant to sodium restriction, is concerning. The literature has been inconclusive, in normotensive and hypertensive patients, about whether sodium restriction worsens insulin resistance. The current study investigated the effect of varying levels of sodium restriction on blood pressure and insulin resistance in hypertensive patients (n = 12).

Subjects were admitted to a research ward and after seven days on a normal diet (200 mmoL sodium), insulin resistance was measured by the euglycemic hyperinsulinemic glucose clamp method. Subsequently, patients were subjected to sodium restriction of either moderate (= 100 mmoL/d) or strict (= 30 mmoL/d) degree.

The change from normal diet to moderate sodium restriction produced only a slight increase in renin levels, but no changes in insulin, glucose, norepinephrine, or aldosterone. Strict sodium restriction, on the other hand, resulted in a 41% increase in fasting insulin, and significant reduction of insulin sensitivity. Moderate sodium restriction is associated with minimal perturbation of glucose homeostasis and neurohumors; strict sodium restriction may result in consequential compensations in norepinephrine and insulin sensitivity. ❖

Gomi T, et al. Am J Hypertens 1998; 11(9):1048-1055.

Intensive Blood-Glucose Control with Metformin

The united kingdom prospective Diabetes Study (UKPDS) has reported recently in its prospective trial (n = 4075) that intensive blood glucose control with sulphonylureas or insulin reduces risk of microvascular complications. A subgroup of this population (n = 753) was followed for over 10 years comparing diet control with metformin; additionally, the metformin recipients were also compared with patients receiving sulfonylureas or insulin for tight control. A final subgroup analysis allowed patients who had not achieved optimum glucose control on maximum sulfonylurea dose to either add metformin, or continue on their same regimen.

The metformin treatment group enjoyed a number of benefits when compared with conventional (standard dose sulfonylurea or insulin) therapy: 36% lower all-cause mortality, 42% lower diabetes-related mortality, and 32% lower incidence of any diabetes-related endpoint. Patients who had metformin added to their regimen of sulfonylurea due to inadequate glucose control did not demonstrate improvements in mortal endpoints, but did trend toward better hemoglobin A-1-C levels, and did not gain as much weight. These data support consideration of metformin as first-line therapy in Type 2 diabetes. ❖

UK Prospective Diabetes Study Group. Lancet 1998;352:854-865.

Low-Dose Hydrocortisone for Treatment of Chronic Fatigue Syndrome

The definition of chronic fatigue syndrome (CFS) includes new onset of severe, unexplained fatigue for at least six months, plus at least four of the following symptoms: memory/concentration deficits, sore throat, tender lymph nodes, muscle pain, multijoint pain, new headaches, unrefreshing sleep, and prolonged postexertional malaise. There has been some literature documentation of reduced cosyntropin responsiveness in CFS patients (30% less cortisol response over 24 hours). Since this aberration suggests a role of insufficient cortisol in CFS patients, McKenzie and associates undertook a randomized trial of low-dose hydrocortisone for CFS (n = 70).

Patients received 20-30 mg hydrocortisone each morning, and 5 mg each evening for 12 weeks. Patients recorded symptoms and well-being on several different scales. The trial was blinded and placebo controlled.

Cortisone therapy was associated with modest symptomatic improvement in some, but not all measurement tools. One-third of cortisone recipients had measurable adrenal suppression secondary to treatment. McKenzie et al conclude that though cortisone treatment did produce some favorable changes, the consequences and frequency of adrenal suppression are too great to consider this therapy appropriate for clinical use. ❖

McKenzie R, et al. JAMA 1998; 280:1061-1066.

Regular Tachycardia in a 42-Year-Old Man

By Ken Grauer, MD

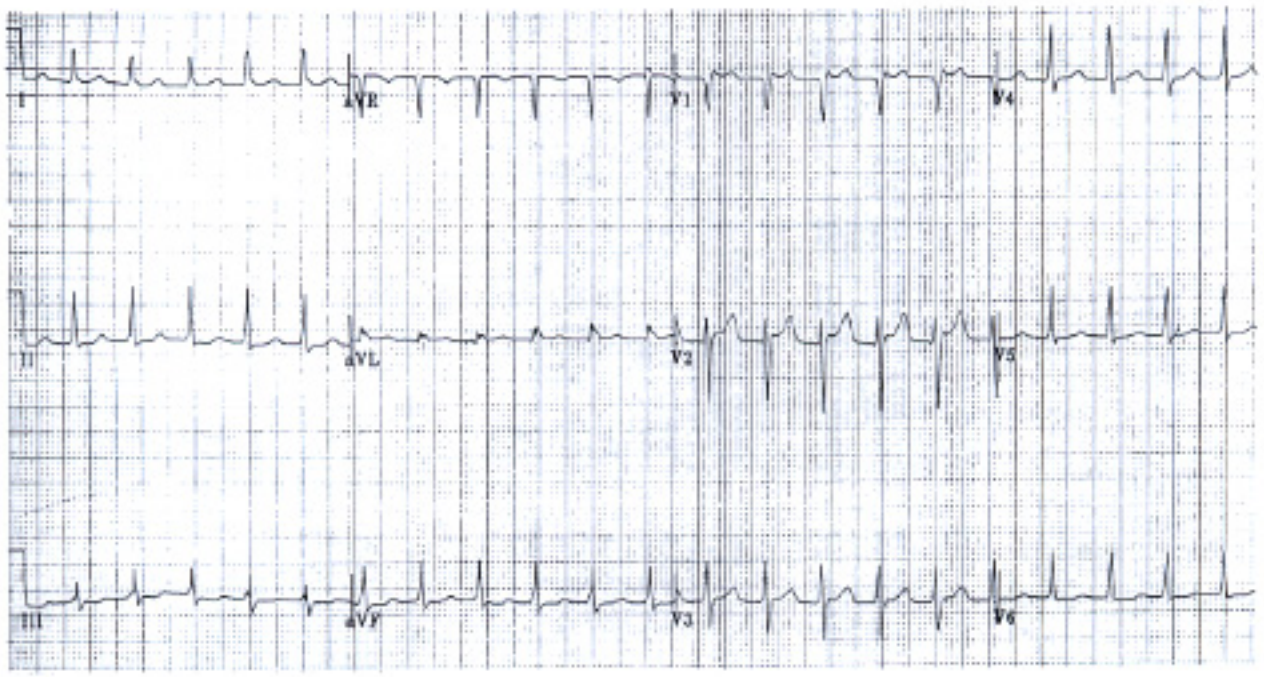

Figure. 12-lead ECG obtained from a 42-year-old man complaining of chest discomfort.

Clinical Scenario: The ECG shown in the Figure was obtained from a 42-year-old man complaining of atypical chest discomfort intermittently over the past few weeks. The patient was previously healthy. He was symptomatic at the time this tracing was recorded. What entities should be considered in your differential diagnosis? Is there evidence of atrial activity in the Figure?

Interpretation: There is a regular, supraventricular tachycardia (SVT) at a rate of just under 150 beats/minute. Practically speaking, the differential diagnosis of a regular SVT at this rate consists of three entities: 1) sinus tachycardia; 2) atrial flutter; and 3) PSVT (paroxysmal supraventricular tachycardia). Definitive diagnosis is unfortunately not possible from this single tracing. The rhythm could be sinus tachycardia, with an upright P wave concealed within the T wave seen in lead II. Atrial flutter should always be considered in the differential diagnosis of a regular SVT at a ventricular rate that is close to 150/minute—but the absence of any semblance of flutter activity in all 12 leads on this tracing makes this possibility less likely. Consequently, the most probable diagnosis is PSVT—which we strongly suspect because of the suggestion of subtle *retrograde* (negative) atrial activity that appears to be notching the terminal portion of the QRS complex in each of the inferior leads, and which produces a terminal positive deflection (simulating an r') in lead V_1. ❖

In Future Issues:

Tolcapone Tablets
(Tasmar-Roche Pharmaceuticals)