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St. John's Wort for Depression: A Systematic Review

ABSTRACT & COMMENTARY

Synopsis: *Using strict criteria, a literature search identified eight studies that examined the efficacy and safety of St. John's wort. These studies provide evidence that St. John's wort is more effective than placebo in the treatment of mild to moderate depression.*

Source: Gaster B, Holroyd J. *Arch Intern Med* 2000;160:152-156.

In order to address whether st. john's wort is useful, Gaster and colleagues systematically reviewed the literature. Gaster et al chose strict criteria for studies to be included in the analysis. Studies had to be 1) randomized, controlled, and double blinded; 2) limited to patients with depression; 3) had to test St. John's wort alone and not in combination with other antidepressants; and 4) had to present original data. Articles meeting these criteria were than reviewed to make sure they were methodologically sound. Of the initial 388 citations, only eight studies met both the inclusion criteria and were felt to be methodologically sound. In six of the eight trials, the dose was 300 mg three times daily of 0.3% hypericum extract.

Of the four studies testing hypericum extract against placebo, all found significant improvement in Hamilton depression scale (HAMD) scores. Four studies tested hypericum extract in comparison to tricyclic antidepressants. These studies were marred by the use of low doses of TCAs which may have reduced the response rate for patients on TCAs. Even so, in these studies, TCAs were slightly more effective than hypericum or similar in efficacy.

Hypericum was generally well tolerated. The most frequently reported side effects were nausea, rash, fatigue, restlessness, and photosensitivity. Among these, the most common side effects were nausea (0.6%) and rash (0.5%). Only 1.2% of patients in the eight studies had to discontinue hypericum because of side effects. In five of the eight studies, laboratory monitoring was performed and there were no changes in cell counts, liver function tests, or creatinine.

INSIDE

Volume 22 • Number 7 • April 15, 2000 • Pages 49-56

COMMENT BY MARTIN LIPSKY, MD

Depression is one of the most commonly encountered problems in primary care. One barrier to treatment is the resistance of many patients to prescription medications. For many individuals, an increasingly popular alternative is St. John's wort that is available as an over-the-counter preparation. Many of our patients are either taking St. John's wort or want to know more about it.

Unfortunately, there are only a paucity of good studies that examine the effectiveness of St. John's wort. This paper, which reviewed the available literature, suggests that St. John's wort is effective for mild to moderate depression. Particularly impressive is the side effect profile. However, despite the few side effects noted, recent articles indicate that St. John's wort may have drug interactions with medications such as digoxin.[1,2]

Proponents argue that St. John's wort is a low-cost alternative for patients with mild depression. However, before it becomes a first-line agent, more information is needed to determine its role among the various agents available for treating depression. For example, no study has compared it to better tolerated antidepressants such as SSRIs. In addition, the lack of standardization among the different preparations remains an obstacle for recommending its use. Still, it may have a role for patients who view it as a more acceptable medication or who cannot afford or tolerate standard antidepressants. ❖

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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.

VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.

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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

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

Multiple Copies

1-9 additional copies: $197 each; 10 or more copies: $175 each.

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Internal Medicine Alert has been approved by the American Academy of Family Physicians as having educational content acceptable for prescribed credit hours. This volume has been approved for up to 40 prescribed credit hours. Term of approval covers issues published within one year from the beginning distribution date of January 1, 2000 with option to request yearly renewal. Credit may be claimed for one year from the date of this issue. The program is also approved by the American Osteopathic Association for 40 Category 2B credit hours.
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The MERIT of Using Metoprolol CR/XL in Heart Failure

ABSTRACT & COMMENTARY

Synopsis: *This study convincingly demonstrates that controlled-release/extended-release metoprolol succinate (metoprolol CR/XL) given once daily is profoundly beneficial to patients with NYHA class II-IV systolic heart failure.*

Source: Hjalmarson A, et al. *JAMA* 2000;283:1295-1302.

During the period of 1996-97, several studies demonstrated that treatment of congestive heart failure with either carvedilol or bisoprolol (both beta-1 blockers) improved survival. On the basis of these observations, the Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF) study was designed to further investigate the survival benefit of beta-1 blockade in chronic heart failure due to systolic dysfunction and to gain information regarding its effect on hospitalizations, symptoms, and quality of life.

The trial was a randomized, double-blind, placebo-controlled trial that recruited patients with NYHA functional class II-IV heart failure. Extended-release metoprolol (metoprolol CR/XL) was compared to placebo. A total of 3991 patients were recruited from 313 investigational sites in the United States and Europe. To qualify, patients had to have ejection fractions of 0.4 or less and be receiving optimum treatment for at least two weeks prior to entry. Optimum treatment was defined as the combination of an ACE inhibitor and a diuretic. If an ACE inhibitor could not be tolerated, hydralazine, a

long-acting nitrate, or an angiotensin II blocker could be used. The patient may or may not have also been receiving digitalis. Furosemide was used as the diuretic (average dose = 65 mg/day) and either enalapril (average 15 mg/day), captopril (70 mg/day), or lisinopril (16 mg/day) was used as the ACE inhibitor.

Patients with class II heart failure were started at 25 mg of extended-release metoprolol per day. Class III-IV patients were started at 12.5 mg. It was recommended that the dose be doubled every two weeks to reach a target level of 200 mg, but the regimen could be modified upon the judgment of the investigator. Once at the target level, patients were followed every three months. Randomization was begun on Feb. 14, 1997, and the last patient was randomized on April 14, 1998. Although it was planned to continue the study for at least 2.4 years of follow-up, the study was stopped on October 31, 1998, due to the significant difference in end points between the treated and nontreated groups.

Treatment with metoprolol CR/XL significantly reduced all combined end points, which included: total mortality or all-cause hospitalization; total mortality or hospitalization due to worsening of heart failure; death or heart transplantation; cardiac death or nonfatal acute myocardial infarction; and total mortality or hosptalization or emergency department visit due to worsening of heart failure. Treatment reduced total mortality by 34% and total hospitalization by 36%. The treatment group also reported a statistically significant improvement in quality-of-life parameters (activities of daily life and sense of well-being).

COMMENT BY MICHAEL K. REES, MD, MPH

This study convincingly demonstrates that controlled-release/extended-release metoprolol succinate (metoprolol CR/XL) given once daily is profoundly beneficial to patients with NYHA class II-IV systolic heart failure. This treatment is also profoundly beneficial to society because expensive hospital days were reduced by 34% by a relatively inexpensive drug. The study greatly challenges at least this practitioner, because at least in the Boston area, the vast majority of managed care plans exclude metoprolol CR/XL from their preferred formulary and request that metoprolol be used instead. The cost to the patient is much greater if the extended-release form of the drug is used.

Are the managed care companies justified in their prejudice against metoprolol CR/XL? Is the practitioner justified in asking the patient to bear a significant increase in out-of-pocket expense for the extended-release/contolled-release formulation? Sandberg and colleagues state: "This formulation leads to a more pronounced and even beta-blockage over 24 hours compared with conventional immediate-relases metoprolol tartrate tablets, 50 mg 3 times per day."[1] The citation here is a paper published in a supplement of the *European Journal of Clinical Pharmacology*. Here it is important to note that the MERIT-HF study was funded by the manufacturer of metoprolol CR/XL.

That metoprolol CR/XL greatly benefits the appropriately selected patient with heart failure seems well established. Whether it does a better job than the much less expensive immediate release form is not established by this study. It will take a head-to-head trial to determine this. Such are the challenges the clinician faces in this era of managed care. ❖

Reference

1. Sandberg A, et al. *Eur J Clin Pharmacol* 1988; 33(suppl):S3-S7.

Does a High Salt Intake Increase Your Risk for Stroke?

ABSTRACT & COMMENTARY

Synopsis: *An increased intake of dietary sodium is associated with an increase in the incidence of cardiovascular disease in overweight persons but not in nonoverweight persons.*

Source: He J, et al. *JAMA* 1999;282:2027-2034.

There are a number of studies that have identified a positive relationship between dietary intake of sodium and increases in hypertension and stroke. However, there are prospective cohort studies that failed to find an association between sodium intake and the risk of stroke. He and colleagues believe that "this may have been due to difficulties in measuring an individual's usual sodium intake or the use of relatively small samples."[1,2]

This prospective cohort study was designed to examine the risk of cardiovascular disease associated with dietary sodium intake in overweight and nonoverweight persons. The study included those aged 25 to 74 years from the first National Health and Nutrition Examination Survey Epidemiological Follow-up Study (NHANES1). Follow-up studies were conducted in 1982-1984, 1986 and 1987, and 1992. (113,467 person-years). The study excluded individuals who: lacked 24-hour dietary recall information, had a history of heart attack or stroke, had used medication for heart disease, or were on a low-sodi-

um diet. A total of 2688 overweight persons and 6797 nonoverweight persons were included.

A body mass index of 27.8 kg/m^2 or higher for males and 27.3 mg/kg^2 or higher for females was used to separate the overweight persons from the nonoverweight.

Sodium intake and total energy intake were highly correlated in the study population. Therefore, both the absolute sodium intake and sodium-to-energy ratio were used to examine the relationship between sodium intake and cardiovascular disease risk.

Sodium-to-energy ratio was expressed as 1 mmol of sodium per 7452 kJ, the average intake in the study population.

Among overweight persons, a 100 mmol higher sodium intake was associated with a 32% increase in stroke, an 89% increase in stroke mortality, a 44% increase in heart disease mortality, and a 39% increase in mortality from all causes. The P values were less than 0.001 in all instances.

Dietary sodium was not significantly associated with cardiovascular disease in nonoverweight persons.

The study concluded that a high sodium intake is strongly and independently associated with an increased risk of cardiovascular disease and all-cause mortality in overweight persons.

COMMENT BY RALPH R. HALL, MD, FACP

He et al also divided the study group into four quartiles and demonstrated that the higher the intake of sodium, the greater the risk of an event. For instance, the cumulative mortality of stroke at age 85 was 9%, 8.9%, 14.4%, and 15. 8% among patients within the first, second, third, and fourth quartiles of sodium-to-energy ratio, respectively (P = 0.004 for trend). This held true for the other risk factors.

There was also an increase in blood pressure noted with an increase in sodium intake but, interestingly, the increase in stroke is greater than one would expect from this degree of blood pressure increase. This suggests, as other studies have, that sodium has an independent effect on stroke incidence.

It therefore behooves us to attempt to decrease the sodium intake of our obese patients. If we are not totally successful, any decrease in sodium intake that the patient is able to achieve will have a beneficial effect on the patient's incidence of cardiovascular disease. African-American patients, because of their low renin levels, should be placed on low-salt diets regardless of their degree of obesity.[3]

This clinical trial required a large number of patients in order to demonstrate the effect of sodium on cardiovascular disease. The numbers of persons needed for clinical trials in the future will be much smaller. This will be because of our ability to identify genetic influences in the molecular structure of our patients' proteins. We can then target patients with the protein structures that are responsible for the condition we are attempting to influence. Our ability to select patients who will benefit from dietary manipulation or specific pharmacologic treatment will be markedly enhanced. As suggested by Herbert,[4] many of the arguments regarding whether patients should have a low- or high-carbohydrate diet or a low- or high-sodium diet, etc., will be facilitated if we place a layer labeled "Genetics" at the bottom of the food pyramid. ❖

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Diabetes, Head Trauma, Marriage, and Dementia

ABSTRACTS & COMMENTARY

Synopsis: *Dementia is increased in diabetes, decreased in married individuals, and not increased with the incidence of head trauma.*

Sources: Ott A, et al. *Neurology* 1999;53:1937-1942; Mehta KM, et al. *Neurology* 1999;53:1959-1962; Helmer C, et al. *Neurology* 1999;53:1953-1958.

Diabetes mellitus type 2 (dm) increases the risk of stroke, and persons with stroke are thought to be more likely to develop dementia if they suffer from diabetes. It has been suggested that DM might also be a risk factor of Alzheimer's disease (AD). Among a community-based prospective cohort study based in the Netherlands, 6370 involved participants were screened for DM and dementia, with an average follow-up period of 2.1 years. In approximately 1100 other cases with no follow-up information, dementia status was culled from medical records.

DM was found to nearly double the age- and gender-adjusted risk of dementia in 692 diabetics. The incidence risk of dementia was highest in those requiring insulin treatment and lowest among newly diagnosed or untreated mild cases. DM incidence in men or women was about equal, with no clear trend in age. When the likely cause of dementia and other confounders was evaluated, diabetes was found to increase by twofold the

risk of both dementia in general and AD in particular.

The Rotterdam Study also addressed the possibility of a relationship between mild head trauma and the development of dementia. This arm of the study included 6645 subjects, age 55 and older, who were free of dementia at the onset. Self-report of past head trauma was obtained from this cohort and incident cases of dementia were determined over the 2.1-year follow-up period. A total of 129 subjects developed dementia over this time. In concordance with some past studies, no increased risk of dementia was found as a function of exposure to head trauma with or without loss of consciousness. In contrast to earlier studies by other groups, possession of the APOE-e4 allele was not found to modify the relationship between head trauma and the development of AD.

A French research team examined the issue of whether marital status affected risk of dementia. Helmer and colleagues divided their cohort of 3675 subjects into groups of married/cohabitant, divorced/separated, widowed, and never married. Helmer et al found the relative risk of dementia was increased among the never married relative to the married individuals, and the risk was specifically associated with AD. The risk of dementia was not significantly elevated among widows and divorced subjects. The results remained significant even after taking into account potentially confounding factors such as educational achievement and wine consumption. The analysis did not permit a firm conclusion to be drawn as to whether never married persons were actually at increased risk or married persons enjoyed some protection against the disease.

COMMENT BY NORMAN R. RELKIN, MD

These results warrant further investigation. One previous indication of a possible association between diabetes and AD came from recent studies showing increased advanced glycosylation end products (AGE) in the brain of Alzheimer's patients. Increased AGE expression is found in other end organs that are frequently affected by complications in diabetics. While there are many possible explanations for such an association, further work will be needed to confirm this observation.

The lack of an association between head trauma and dementia in this report is not surprising, in that five out of every six studies of head trauma and dementia carried out before 1990 failed to demonstrate just such a relationship. However, more recent work has suggested an additive or even synergistic relationship between head trauma, dementia, and APOE genotype. The negative findings in this case may, in part, reflect differences in the method of ascertainment of head trauma history or another unrecognized confounding factor.

Failure to marry has not been previously implicated as a risk factor for AD. Helmer et al made a valiant effort to measure the subjects' social involvement independent of marriage, and found that level of social activity did not correlate with dementia incidence. One could postulate similar protective mechanisms for marriage as for higher education. An alternative explanation is that unmarried persons have some underlying personality trait that segregates with the propensity to develop dementia. Whatever the explanation, it's somewhat comforting to know that the much-maligned institution of marriage may have benefits above and beyond joint tax returns. *(Dr. Relkin is Associate Professor of Clinical Neurology and Neuroscience at New York Presbyterian Hospital-Cornell Campus.)* ❖

Pharmacology Update

Pantoprazole Delayed-Release Tablets (Protonix-Wyeth Laboratories)

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

With astrazeneca's omeprazole (prilosec) holding firm as the best-selling medication in the world, other pharmaceutical companies are rushing to develop their own proton pump inhibitors (PPIs). The latest entry into the market is pantoprazole (Protonix—Wyeth Laboratories), the fourth PPI to be approved by the FDA for use in this country. Pantoprazole is a benzimidazole derivative chemically similar to omeprazole and lansoprazole. The drug is licensed from Byk Gulden Pharmaceuticals in Germany and marketed as Protonix by Wyeth. The drug was approved for the treatment of reflux esophagitis. A parenteral form is awaiting FDA approval.

Indications

Pantoprazole is approved for short-term treatment in the healing and symptomatic relief of erosive esophagitis. The recommended course of treatment is up to eight weeks. If healing has not been achieved after eight weeks, an additional eight-week course may be considered.[1]

Dosage

Pantoprazole is available as 40-mg delayed-release (enteric-coated) tablets. The recommended adult dose is 40 mg daily for up to eight weeks. It may be taken with-

out regard to meals or antacids.[1] No dosage adjustment is needed for patients with mild to severe renal impairment, mild or moderate hepatic impairment, or in elderly patients. The tablets should not be split, chewed, or crushed, as an enteric coating protects the acid labile pantoprazole from the low gastric pH.

Potential Advantages

Pantoprazole has low affinity for cytochrome P450 isoenzymes. Clinically significant drug interactions necessitating dose adjustments have not been reported with any of the following drugs: theophylline, cisapride, carbamazepine, diazepam, diclofenac, digoxin, glyburide, levonorgestrel/estradiol, metoprolol, nifedipine, phenytoin, or warfarin.[1,2]

Potential Disadvantages

As with other antisecretory drugs, pantoprazole may interfere with the absorption of drugs that depend on gastric acid for absorption (e.g., ketoconazole, iron salts). Maintenance use of pantoprazole beyond 16 weeks has not been established.[1] Clinical experience is limited with pantoprazole.

Comments

Pantoprazole is the newest PPI to be approved by the FDA. It is only approved for the healing and symptomatic relief of erosive esophagitis. Similar to omeprazole and lansoprazole, it is an irreversible inhibitor of the parietal cell H+, K+ ATPase. In a U.S. multicenter, double-blind, placebo-controlled trial, pantoprazole produced a healing rate of 75% at four weeks and 92.6% at eight weeks compared to 14.3% and 39.7% for placebo.[1] A comparative trial with omeprazole indicated comparable efficacy in healing and symptom relief of reflux esophagitis.[2] Although pantoprazole is not FDA approved for the treatment of gastric ulcers, duodenal ulcers, or the eradication of *H. pylori*, data suggest that its efficacy in these conditions is similar to other PPIs. PPIs also have similar side effect profiles, with diarrhea and headache as the most frequent side effects among the various agents.[3]

Pantoprazole is chemically more stable than omeprazole or lansoprazole in a weakly acidic condition (pH 3.5-7.4), which may improve its selectivity for parietal cell H+, K+ ATPase and less stable for less acidic compartments such as lysosomes and chromaffin granules.[2,3] The clinical relevance of this is not known.

Pantoprazole is expected to be available in the second quarter of 2000. Cost is currently not available.

Clinical Implications

Pantoprazole represents the fourth entry into the competitive PPI market where efficacy and side effect profiles are similar among the various agents.[4] Pantoprazole may have two advantages among these agents in that it may be the least likely to interact with other drugs (although drug interactions have generally not been problematic for these drugs).

It will also likely be the first PPI to be available in a parenteral form, which is awaiting FDA approval. The oral and intravenous forms have been reported to be equivalent, on a mg basis, in gastric acid suppression in patients with gastroesophageal reflux disease.[5] ❖

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5. Metz DC, et al. *Am J Gastroenterol* 2000;95:626-633.

CME Questions

22. Which of the following statements is *false*?

a. St. John's wort is effective for mild to moderate depression.
b. St. John's wort is more effective than tricyclic antidepressants.
c. St. John's wort is better tolerated than many other antidepressants.
d. St. John's wort is an inexpensive alternative for treatment of mild to moderate depression.

23. Which one of the following statements is *not* correct?

a. Obese patients are more likely than nonobese patients to benefit from a low-sodium diet.
b. The higher the sodium intake, the greater the chance for a cardiovascular accident.
c. The hypertension resulting from a high sodium intake is solely responsible for the increase in cardiovascular events.
d. Even small decreases in sodium intake may reduce cardiovascular events.

24. In the MERIT-HF study, what is the recommended starting dose of Metoprolol CR/XL for the patient with NYHA class III systolic heart failure?

a. 6.25 mg/day
b. 12.5 mg/day
c. 25 mg/day
d. 37.5 mg/day

25. Which is *not* true about pantoprazole?

a. It is approved for the treatment of peptic ulcer disease and Zollinger-Ellison syndrome.
b. It is taken once a day.
c. It has a low incidence of drug interactions.
d. There is a parenteral form of the drug that is awaiting approval.

By Louis Kuritzky, MD

Efficacy and Safety of the Oral Neuraminidase Inhibitor Oseltamivir in Treating Acute Influenza

Agents that have been shown to be efficacious only against type A viruses have limited treatment of influenza. The recent introduction of neuraminidase inhibitors, which are effective against influenza A and influenza B viruses, offer new breadth of antiviral activity. This study evaluated a large population (n = 629) of nonimmunized adults who were subject to spontaneous acute febrile respiratory illness. Inclusion criteria included no influenza vaccination for at least 12 months, overall good health, symptoms present for less than 36 hours, and temperature of at least 38°.

Treatment consisted of oseltamivir (Tamiflu) 75 mg or 150 mg orally twice daily vs. placebo. Participants were allowed to use acetaminophen for symptomatic relief, and their use of acetaminophen was quantified.

Overall duration of illness was reduced by more than 30% with oseltamivir treatment. Similarly, symptom scores were significantly improved with active treatment so that median severity of illness decreased by approximately 40%. Improvements in symptoms were notable as early as 24 hours after administration of the first dose. Fever was significantly reduced within 24 hours also, and persons who received oseltamivir used approximately 20% less acetaminophen for symptom relief. There were no serious clinical or laboratory side effects seen, and the withdrawal rate was the same as or less than placebo.

Oseltamivir is effective and well tolerated in treatment of acute influenza A or B. ❖

Treanor JJ, et al. JAMA 2000;283: 1016-1024.

Self-Reported Arthritis-Related Disruptions in Sleep and Daily Life and the Use of Medical, Complementary, and Self-Care Strategies for Arthritis

Despite evolution in arthritis management tools, arthritis remains the most common cause of disability in persons older than age 65. Using the population of subjects participating in the National Follow-up Survey of Self-care and Aging (n = 3485), Jordan and colleagues selected 1925 individuals for evaluation in this trial. The purpose of the study was to examine the effects of arthritis on use of self-care, complementary therapies, and traditional medical care.

More than half of these persons reported that arthritis had limited their activities in the previous year, including sleep and leisure activity disruption in approximately one-third.

Typical management strategies included over-the-counter remedies (topical and systemic agents), physician consultation, local physical therapies (e.g., heat, cold, massage), rest, and prayer, each of which was used by at least 40% of the arthritis sufferers. Persons with sleep disruption due to arthritis were much more likely to seek physician consultation (odds ratio = 3.66) than those without.

The importance of disrupted sleep as a consequence of arthritis may have been underestimated. Not only is the sleep disruption of immediate consequence, it increases the likelihood of use of a variety of other self-care and health professional resources. Clinicians are encouraged to consider increasing their attention to sleep disruption as a consequence of arthritis. ❖

Jordan JM, et al. Arch Fam Med 2000;9:143-149.

Estrogen Replacement Therapy for the Treatment of Mild to Moderate Alzheimer's Disease

Since women live longer than men, and Alzheimer's disease (AD) risk increases with advanced age, the problem occurs with twice the frequency in women. Whether estrogen replacement therapy (ERT) has an effect on AD has been an issue of some debate, and though initial impressions have been positive, the literature has not been definitive. Mulnard and colleagues selected 120 women with mild to moderate AD who had also recently undergone hysterectomy, thus eliminating concern for induction of endometrial hyperplasia by ERT. These women received either 0.625 mg or 1.25 mg estrogen daily for 12 months, or placebo.

Several tools were used for measuring outcome, including the Clinical Global Impression of Change scale (CGIC), the Clinical Dementia Rating Scale (CDR), the Ham Depression Scale, and the Multiple Effect Adjective Checklist. Multiple measurement tools for memory were also included.

There were no measurable persistent effects of ERT on any of the measured parameters, though there was a transient Mini Mental Status Examination improvement. Mulnard et al conclude that ERT therapy does not prevent progression of or improve the status of AD, and comment that the adoption of ERT for AD prior to randomized trials demonstrating its benefit is reason for concern. ❖

Mulnard RA, et al. JAMA 2000;283: 1007-1015.

A Question-Inducing SVT

By Ken Grauer, MD

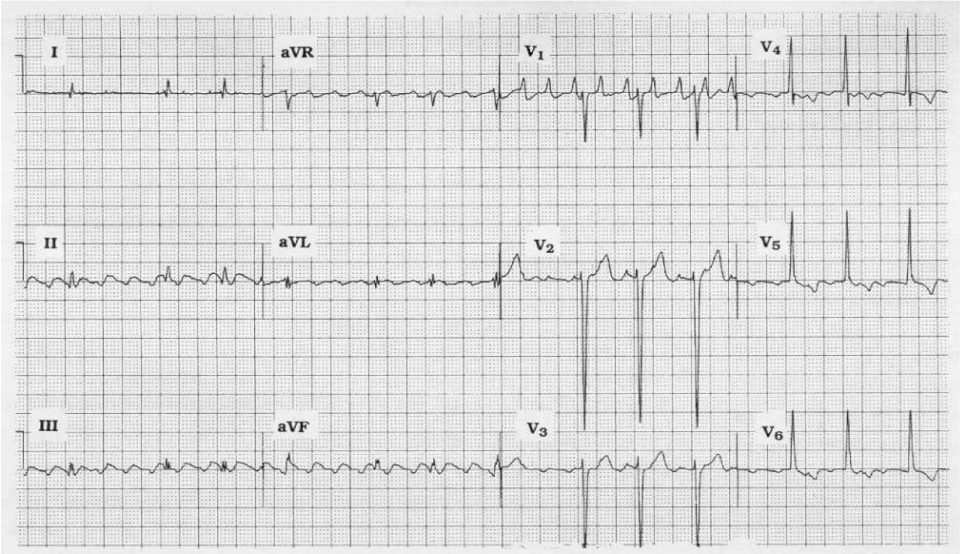

Figure. 12-lead ECG obtained from a 57-year-old man.
What questions should be raised in your mind by interpreting this tracing?

Clinical Scenario: The 12-lead ECG shown in the figure was obtained from a 57-year-old man. Review of this ECG should raise (induce) several questions in your mind. Which questions? Answer this even though you have not been provided with any clinical information about the patient.

Interpretation: The ventricular rhythm is irregularly irregular. A supraventricular etiology is confirmed by recognition that the QRS complex is narrow in all 12 leads. Despite the irregularity, this rhythm does not represent atrial fibrillation because organized atrial activity is present. Instead, the regular sawtooth pattern of atrial activity in the inferior leads identifies the rhythm as atrial flutter. The first unusual point about this tracing is the exceedingly large amplitude of the pointed flutter waves in lead V_1. The second unusual point is the rate of flutter activity, which at 220/minute is clearly slower than the usual atrial range for flutter. This raises the first question, which is whether the patient might be taking any drug(s) that may act to slow the flutter rate (i.e., antiarrhythmic agents such as quinidine or amiodarone—or AV nodal blocking drugs such as verapamil or diltiazem). Although the most common ventricular response to atrial flutter is with 2:1 AV conduction, followed by 4:1 AV conduction—a *variable* ventricular response (as occurs here) may also often be seen.

The second question raised on interpreting this tracing is whether the patient has had an inferior infarction. Although QRS amplitude is markedly reduced in all six limb leads—small q waves do appear to be present in leads II, III, and aVF. Assessment for ST segment changes in these inferior leads is impeded by a relatively large amplitude of flutter activity, thus making it impossible to comment on the acuity of inferior changes.

A final question raised by interpreting this tracing relates to the meaning of ST segment changes in the lateral precordial leads. The very deep S wave in lead V_2 strongly suggests left ventricular hypertrophy (LVH). We suspect ST changes in leads V_4, V_5, and V_6 represent repolarization changes of LVH (i.e., "strain")—but simultaneous occurrence of flutter activity makes it difficult to verify this assumption. ❖

In Future Issues:

Orlistat as an Adjunct to Obesity Therapy in Primary Care