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# PSYCHIATRIC MEDICINE IN PRIMARY CARE™

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## Gabapentin vs. Propranolol for Essential Tremor

ABSTRACT & COMMENTARY

**Source:** Gironell A, et al. A randomized placebo-controlled comparative trial of gabapentin and propranolol in essential tremor. *Arch Neurol* 1999;56:475-480.

ESSENTIAL TREMOR (ET), ONE OF THE MOST COMMON MOVEMENT disorders, is characterized by tremor during the maintenance of posture and active movement. Although ET is commonly perceived to be benign, some patients suffer significant disability, and a larger number suffer substantial embarrassment.

The efficacy of primidone and B-adrenergic antagonists (e.g., propanolol) has been demonstrated, but many patients fail to respond, suffer intolerable side effects, or have contraindications to these medications. Previously, an open-label trial of gabapentin (Neurontin) suggested efficacy for ET,[1] but a double-blind, placebo-controlled study of adjunctive gabapentin in 20 patients found no improvement at a dose of 1800 mg/d compared to placebo.[2] The current study was undertaken in the neurology clinic in Barcelona, Spain. Sixteen patients with moderate to severe bilateral ET and no other neurological disorders were enrolled. Exclusion criteria included cardiac failure, asthma, peripheral vascular disease, diabetes mellitus, and active treatment with tremor-inducing or alleviating drugs.

After a two-week washout period, participants were given gabapentin 400 mg tid or propranolol 40 tid for two weeks in a double-blind, placebo-controlled, crossover trial. A one-week washout period occurred between treatments. Assessment measures included the Tremor Clinical Rating Scale (TCRS), accelerometric (neurophysiological) recordings done on the index finger of the most affected hand, and a 25-item self-reported disability scale. The TCRS includes four examinations rated on a 0-4 scale: 1) tremor of the hands, legs, head, and trunk; 2) motor task performance; 3) functional disability; and 4) subjective assessment by the patient. Analysis of variance (ANOVA) was used to test the effect of medication



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on tremor. Paired comparisons were analyzed by the test after control for inflation type I errors.

A statistically significant treatment effect was shown for gabapentin and propranolol compared to placebo with regard to tremor, motor task performance, functional disability, and subjective assessment by the patient on the TCRS. No statistical differences were found between gabapentin, propranolol, and placebo in terms of the accelerometric (neurophysiological) recordings; baseline variability may have been too great to see a treatment effect. In terms of the self-reported disability scale, neither drug was statistically better than placebo. All patients completed the study; no serious adverse events occurred. Limitations included a small sample size, fixed dosing (which limited meaningful titration), performing accelerometric recordings only on the most affected hand (potential bias, rather than an average of both hands), and a single study site (which limits generalization of the results).

### COMMENT BY DONALD M. HILTY, MD

The origin of ET is unknown. A central mechanism involving the inferior olive is incriminated by most experimental data,[3] though some modulation may occur from the cerebellum, thalamus, motor cortex, and brainstem nuclei.[4] Gabapentin may work by increasing gamma-aminobutyric acid (GABA) levels and reducing intracortical excitability. Gabapentin is extremely well tolerated, even in geriatric patients.[5] A large, multicenter trial is indicated to further study gabapentin for ET. ❖

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# Venlafaxine for Diabetic Neuropathy

ABSTRACT & COMMENTARY

**Source:** Davis JL, Smith RL. Painful peripheral diabetic neuropathy treated with venlafaxine HCl extended release capsules. *Diabetes Care* 1999;22(11):1909-1910.

DESPITE MANY ADVANCES IN THE TREATMENT OF DIAbetes mellitus, diabetic neuropathy (DN) remains a common clinical dilemma. Even when maintaining tight glycemic control, patients may develop DN, which can be difficult to treat. Pharmacotherapy for DN involves many different types of agents, including aldose reductase inhibitors, mexiletine, capsaicin, gabapentin, carbamazepine, and tricyclic antidepressants (TCAs). However, in many cases these medications either fail to provide adequate relief or are difficult to tolerate. The current series of cases suggest that extended release venlafaxine (Effexor XR) may be useful in the treatment of DN.

The first case involved a 41-year-old man who was diagnosed with diabetes after presenting with mild nocturia. He was found to have blood glucose levels of approximately 200 mg/dL. Approximately seven months after treatment with dietary modification and glipizide 10 mg/d, he developed severe burning paresthesia around the mid-tibial region, necessitating that he not wear shoes. He experienced no relief from aceta-

minophen, codeine, or amitriptyline. The patient was started on venlafaxine extended release capsules at 75 mg/d and experienced 95% relief within five days. The pain recurred five days after discontinuing venlafaxine and remitted once again approximately three days after restarting the drug.

Due to the remarkable response shown in this patient, 10 additional patients (age 35-71) were initiated on venlafaxine 37.5-75 mg/d. The duration of diabetes for this group varied from 2-25 years. All patients had been treated with oral hypoglycemics alone or in combination with insulin. All patients, who had failed previous trials of medications such as TCAs, experienced approximately 75-100% reduction in pain within 3-14 days after the initiation of venlafaxine. Extended release venlafaxine was well tolerated by all subjects.

### COMMENT BY MICHAEL F. BARBER, PharmD

The current article suggests that venlafaxine extended release capsules may be effective and well tolerated in the treatment of DN. Since this was a nonrandomized study, a placebo response cannot be ruled out. However, the reported results were striking, especially since the participants had failed previous trials of other agents. Venlafaxine is an antidepressant that inhibits the reuptake of serotonin, norepinephrine, and, to some extent, dopamine, in a dose-dependent manner. Tricyclic antidepressants also inhibit the reuptake of serotonin and norepinephrine, but tend to have more side effects because of additional effects on alpha adrenergic, muscarinic, and histaminic receptors. Davis and Smith hypothesized that the patient's mixed neuotransmitter profile is associated with greater efficacy in treating DN compared to prior studies with fluoxetine, which is more selective for serotonin reuptake. However, in the relatively modest doses used in this series, the primary effect of venlafaxine would be inhibition of the reuptake of serotonin. As such, there may be a more complex reason for the differences in response between venlafaxine and fluoxetine if such a difference is indeed demonstrated in head-to-head randomized studies. Venlafaxine is usually well tolerated, particularly when the extended release capsules are used. One of the more concerning side effects of venlafaxine is an increase in blood pressure. This effect is dose-dependent, with clinically important blood pressure increases usually only taking places in doses of 225 mg/d or higher.

In conclusion, while venlafaxine may be effective in the treatment of DN, controlled trials are required before venlafaxine can be considered as a front-line agent. However, venlafaxine should be considered when other agents are unsuccessful in the treatment of DN. ❖

# Paroxetine Vasovagal Syncope

ABSTRACT & COMMENTARY

**Source:** Calkins H. Pharmacologic approaches to therapy for vasovagal syncope. *Am J Cardiol* 1999;84:20Q-25Q.

VASOVAGAL SYNCOPE (VVS) IS A RELATIVELY COMMON disorder involving autonomic cardiovascular dysregulation. VVS typically is not a dangerous disorder, but it can be somewhat disabling in severe cases. Although nonpharmacologic modalities such as salt and fluid loading may be used to treat VVS, many pharmacologic agents have been proposed as effective in the management of this condition. Most of the available data are based on nonrandomized clinical trials. In fact, only atenolol, midodrine, and paroxetine have demonstrated efficacy in the treatment of vasovagal syncope in at least one randomized, placebo-controlled clinical trial. Other therapies commonly used in treating syncope include increased salt and fluid intake and fludrocortisone. In the current review, Calkins provides a summary of currently available data that support or question the use of various pharmacologic agents for treatment of vasovagal syncope.

VVS is thought to be the result of a paradoxic reflex that occurs when reduced venous pooling results in an increase in catecholamines. This increase is followed by mechanoreceptor stimulation throughout the heart and the pulmonary artery. This stimulation results in an abrupt increase in vagal tone. As a result of increased vagal tone, bradycardia and vasodilation occur, which, along with the existing condition of venous pooling, lead to dizziness and syncope. Pharmacotherapy may be targeted at either the efferent limb of the reflex (increased vagal tone or vasodilation) or the afferent limb (increased venous pooling).

Beta blockers are used to treat VVS because they block the increase in catecholamines that result from the increased venous pooling. Despite the fact that there are several reports on the efficacy of beta blockers in the literature, there is only one randomized, placebo-controlled trial (RCT) that supports their use. The study (n = 42) reported that atenolol improved orthostatic hypotension in 62% compared to only 5% of those taking placebo (P = 0.0004). Although other studies were not RCTs, similar results have been exhibited for the other beta blockers. Alpha-1 receptor agonists also may be used to treat VVS by inducing vasoconstriction. The only RCT using midodrine showed efficacy in 16 patients who experienced 7.3 more symptom-free days than those

receiving placebo ($P < 0.0001$). Selective serotonin reuptake inhibitors (SSRIs) may help relieve VVS by down-regulating certain post-synaptic serotonin receptors that are believed to be involved in mediating vasodilation. Paroxetine is the only SSRI that has shown efficacy in an RCT. After one month of therapy with 20 mg/d, 62% of paroxetine-treated patients became symptom-free upon tilt-table testing vs. 38% of placebo-treated patients ($P < 0.0001$). Surprisingly, one of the agents quite commonly used, fludrocortisone, has not been evaluated by an RCT.

**COMMENT BY MICHAEL F. BARBER, PharmD**

The current review supports the use of paroxetine for use in patients with VVS. Ideal candidates would be those who may not be able to tolerate beta blockers (such as asthmatics) or those patients with depression or other disorders for which SSRIs are indicated (obsessive-compulsive disorder, panic disorder, etc.). Notably, there seemed to be a lag in time to onset of therapeutic benefit for SSRI-treated patients compared to other agents (although head-to-head studies have not been performed). This is consistent with the time to onset of relief from depressive symptoms and may be related to the amount of time needed to down-regulate post-synaptic serotonin receptors. In published studies of SSRIs for use in VVS, there were several patients who dropped out due to intolerable adverse effects, suggesting that some patients may need to be titrated more slowly. ❖

# Are Smoking and Panic Attacks Related?

ABSTRACT & COMMENTARY

**Source:** Breslau N, et al. Smoking and panic attacks. *Arch Gen Psychiatry* 1999;56:1141-1147.

Further clarification of the relationship between smoking and panic attacks is important for patient education. For example, daily smoking might cause panic attacks, panic attacks might increase the risk for daily smoking, or, if there is an association between panic attacks and smoking, it might be noncausal: smoking and panic attacks might be linked by a shared etiology. Although observational studies cannot definitively test causal hypotheses, they can dampen the plausibility of some hypotheses and suggest the plausibility of others.

To address this issue, Breslau and colleagues analyzed data from two epidemiological studies: the Epidemiologic Study of Young Adults (ESYA) in southwest Michigan, and the National Comorbidity Survey Tobacco Supplement (NCSTS). Both studies used a structured, lay-administered form of the DSM-III-R for diagnosis. The ESYA (n = 1007) consisted of 21- to 30-year-old members of an HMO, with baseline interviews in 1989 and follow-up interviews in 1990, 1992, and 1994. The study group was 62% female, 80% Caucasian, and 45% married. The NCSTS (n = 4411) interviewed 15- to 54-year-olds at one point. Hazard models with time-dependent covariates were used to estimate the risk for the onset of panic attacks associated with current and prior daily smoking and vice versa. The study controlled for sex and history of major depression, since the latter is associated with both panic attacks and smoking. The influence of heavy drinking was analyzed, given its potential role in panic attacks and its association with smoking, but its inclusion in the model did not alter estimates. The role of lung disease was assessed as a confounding variable that could cause panic attacks.

Baseline characteristics of the population in the ESYA and NCSTS (respectively) were: 42% and 47% smoked daily; 21% and 18% had a history of depression; 12% and 7% had panic attacks; 5% and 3.5% had panic disorder; 13% and 11% smoked daily and had a history of depression; 7% and 3% had panic attacks and a history of depression; and 4% and 2% had panic disorder and a history of depression. In the ESYA database, the lifetime association between panic attacks and daily smoking was similar in both men and women, with odds ratios (ORs) of 3.13 and 2.61, respectively. The hazard ratio (HR) of panic attack associated with prior daily smoking was 3.96. The HR of panic attacks associated with depression alone was 12.98, compared to 12.77 for depression with daily smoking; analyses indicated that if smoking followed the onset of depression, there was an additive effect for the risk of panic attacks. The HR of the first panic attack in daily smokers who continued to smoke was 4.71, compared to 0.21 in those who quit smoking. The HR of smoking after the onset of panic attacks was 1.0. The NCSTS data were more limited in scope. The HR of the first panic attack in daily smokers who continued to smoke was 2.08, compared to 1.85 in those who quit smoking, which is not statistically different. The HR of smoking after the onset of panic attacks was only 1.37. For both data sets, the ORs for panic attacks associated with lung disease, alone and with daily smoking, were higher than for daily smoking alone. The ORs of first panic attack associated with lung disease alone was 9.2, for daily smoking alone was 1.7 (insignificant), and together was 10.7.

The results suggest the possibility that the relationship between smoking and panic attack or disorder might flow primarily in one direction (i.e., from smoking

to subsequent onset of panic attacks or disorder), particularly in active daily smokers. Lung disease is associated with an increased lifetime prevalence of panic attacks in nonsmokers and smokers (with or without lung disease). By increasing the risk for lung disease, smoking might indirectly increase the risk for panic attacks.

### COMMENT BY DONALD M. HILTY, MD

The relationship between depression and smoking is believed to be noncausal, mediated largely or entirely through genetic factors that influence the liability to both smoking and depression.[1] The current study best supports a hypothesis that smoking predisposes a patient to panic attacks, but does not rule out a noncausal relationship similar to that of smoking and depression. One interesting hypothesis posits that panic attacks may represent a suffocation false alarm.[2] Smokers, who often develop pulmonary problems, may be more prone to react to suffocation signals as manifest panic attacks. Carbon monoxide in cigarette smoke might affect the suffocation alarm threshold and/or the asphyxiation monitor for the suffocation alarm system (which may be the carotid body).[3] ❖

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## *Special Feature*

# The DHEA Controversy

*By Dónal P. O'Mathúna, PhD*

The subtitles of recent popular dehydroepiandrosterone (DHEA) books tell it all: *Unlocking the Secrets to the Fountain of Youth*,[1] *Exploring the Link Between Youth & Aging*,[2] and *The Natural Hormone That Helps Fight Disease, Improves Mood & Energy, Boosts Your Sex Drive, and Influences Longevity*.[3] However, the authors of cited clinical research studies report, "The hype is out of control … DHEA is the snake oil of the '90s. DHEA sales could be a disaster in the making."[4] How can a busy physician make sense of these contradictory claims?

### Introduction and Claims

In 1996, the scientist who first isolated the sulfate ester of DHEA (DHEAS) concluded: "Several years will be necessary to pass from precise and limited observation to a sure, efficacious product useable by many people."[5]

DHEA is supposed to slow aging, burn fat, build muscle mass, strengthen the immune system, treat lupus, and help prevent heart disease, cancer, diabetes, and Alzheimer's and Parkinson's diseases.[6] It is also reported to boost libido, alleviate depression, and increase general feelings of strength, stamina, and well-being.[7] It is most commonly self-prescribed as an antidote to the general effects of aging, especially around menopause.[6]

From 1985 to 1994, DHEA was available only by prescription. The 1994 Dietary Supplement Health and Education Act reclassified DHEA as a dietary supplement, allowing it to be sold over-the-counter.

### Pharmacology

DHEA is a steroid hormone, closely related to testosterone and estrogen. DHEA is converted endogenously into DHEAS, the predominant form in the circulation.[5] If taken orally, DHEAS is converted into DHEA in the stomach. Endogenous DHEA is made from cholesterol in the adrenal glands. Fetuses produce copious amounts, but levels drop precipitously at birth, increase again around age six or seven, peak in the mid-20s, and then gradually decline.[8] At its peak, DHEA is the most abundant hormone in the circulation. By the time people are in their 60s, the levels have dropped to 10-20% of their peak values. DHEA levels are lowered by some illnesses, including rheumatoid arthritis and major depressive disorders, and by periods of stress.[9] Levels are increased by smoking and alcohol.[10]

Decreased DHEA levels are accompanied by reduced levels of other steroids, including testosterone and androstenedione.[11] The steroid level that correlates best with chronological age and age-related cognitive and physical deficits is bioavailable testosterone (BT).[11] Most testosterone in the body is tightly bound to globulins, but a small proportion of BT is loosely bound to albumin, making it readily available for use by tissues.[12]

DHEA may play a role in binding albumin molecules, changing their shape, and giving them more affinity for testosterone, thus decreasing the levels of BT.[12] This effect is dose dependent. Administration of moderate amounts of DHEA restored serum DHEA to youthful levels, but did not affect BT levels.[13] High levels of oral DHEA reduced BT levels.[12] Intramuscular administration of testosterone along with moderate doses of DHEA may restore both BT and DHEA to peak levels.

## Clinical Studies

The vast majority of research on DHEA supplements has been conducted on animals. The studies have shown positive effects in preventing cancer, diabetes, heart disease, viral infections, and brain diseases. The relevance for humans is questionable since only humans and a few primates synthesize and secrete DHEA and DHEAS.[10] A 1998 review found 23 clinical investigations of DHEA supplementation since 1966.[10] Many of these studies were unblinded with no control groups. One had 28 subjects, but the others had fewer than 15. Different preparations, doses, and routes of administration were used. The reviewers concluded, "The clinical literature is fraught with problems."[10]

Differences between men's and women's responses have been noted.[14] A 10% DHEA cream was evaluated in 14 women aged 60-70 years, 10 of whom began with completely atrophic vaginal smears.[15] After therapy, eight had vaginal cytology typical of menstruating women, four showed "improvement," and two showed no significant changes. Hip bone mineral density also increased significantly ($P < 0.05$). Eighty percent of the subjects reported an improved sense of well-being, confirming earlier findings.[13]

A study with 22 post-menopausal women studied the effect of DHEAS on serum beta-endorphin levels.[16] Post-menopausal beta-endorphin levels are reduced, and raising them was assumed to correlate with an improved sense of well-being. The subjects were randomly divided into three groups, one receiving oral DHEAS (n = 8; 50 mg/d), the second (n = 8) receiving oral DHEAS (50 mg/d) plus transdermal estradiol (50 µg/patch), and the third receiving transdermal estradiol alone (n = 6; 50 µg/patch). All three therapies showed equivalent restoration of beta-endorphin levels, and the authors concluded this supported the therapeutic efficacy of DHEAS for improving one's sense of well-being.

The first double-blind, placebo-controlled trial of DHEA for major depression was recently reported.[17] Twenty-two patients with major depression were randomly assigned to DHEA (maximum, 90 mg/d) or placebo (n = 11 in each group). Five of those taking DHEA and none of those taking placebo showed at least a 50% reduction in depressive symptoms.

## Formulation and Dosage

Oral administration of 25-50 mg DHEA daily returns most people's DHEA levels to their youthful peaks.[5] But optimal dosages are difficult to determine for numerous reasons. Healthy people of similar age have DHEAS blood levels that vary more than threefold, and no correlation exists between these levels and overall health or life expectancy.[5] Dosage determinations are also complicated by conditions causing DHEA levels to fluctuate (some are listed under "Pharmacology").

DHEA is often sold in precursor form, usually as plant extracts (wild yams and soy), with accompanying claims that the plant steroids are converted into DHEA. Humans have no metabolic pathway to accomplish this long, complex synthesis, making it unlikely these products affect blood DHEA levels.[8] Lack of regulation is another problem. One review found commercial products contained 0-150% of the labeled amount.[18] Nine of the 16 products failed to meet standard pharmaceutical specifications of 90-110% of labeled amount.

## Adverse Effects

Some women taking DHEA stop menstruating, grow body and facial hair, and develop deeper voices.[7] DHEA has been reported to decrease HDL cholesterol levels in women, though not in men.[14]

The association between DHEA and breast cancer risk is complex. A study with 213 women not taking DHEA supplements (mean age, 62 years) found postmenopausal women with elevated levels of endogenous estradiol, testosterone, and DHEA had an increased risk of breast cancer.[19] However, when the results for all three hormones were analyzed together, the influence of DHEA was reduced by 83%.

In men, an increased testosterone level could enlarge the prostate, interfering with urination, or stimulate growth of prostate cancer, although reports of this were not found.[7] A recent study found no changes in the prostate or in PSA levels.[16] At low concentrations, DHEA protected in vitro liver cells against lipid peroxidation, but at slightly higher concentrations it promoted oxidation.[20]

## Conclusion

DHEA is a natural steroid hormone but its natural function remains unclear. Its role in human metabolism is widespread, but poorly understood. It is not a typical hormone because its receptor has not yet been found (if it has one). Its effect may have more to do with its metabolites than its native form. It is widely involved in human metabolism, but precisely how is poorly understood. Its efficacy and long-term safety in treating age-related medical problems remain unclear, although recent evidence suggests promise in diseases of hormonal regulation.

## Recommendation

It is premature to recommend using DHEA supplements for relief of menopausal symptoms, though short-term use does seem to improve people's sense of well-being. Since DHEA is associated with many divergent

metabolic processes, the chances for adverse effects are high. However, DHEA is the subject of active clinical investigation and some results are encouraging. Until the results of larger, long-term studies are available, DHEA supplementation cannot be recommended as an evidence-based therapeutic option in menopause. *(Dr. O'Mathúna is Professor of Bioethics and Chemistry at Mt. Carmel College of Nursing, Columbus, OH.)* ❖

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## *Special Feature*

# Tips for Searching PubMed

*By Leah Anderson, MLS*

***Editor's Note**: This is the second in a series of articles on using PubMed, the National Library's search service, which includes Medline. It is free via the Internet and can be found at www.nebi.nlm.nih.gov/PubMed.*

All literature database strategies involve a balance between the number of references retrieved and the relevancy of the results to the question at hand. For many librarians, a good search is one in which the vast majority of the references found address the requester's question. We are more confident that all references on that topic were retrieved because the search was performed broadly enough to pick up a bit off the topic. If the search yielded only references directly on the topic, then one worries that something was missed. The following are tips for searching the PubMed database that can improve relevancy over retrieval.

Never search for your terms using the parameter "All Fields." Unfortunately, "All Fields" is the default setting in PubMed. You have to manually change it to something else but your searches will be more focused. There are many fields in a PubMed record that have nothing to do with the topical content of the article. Thus, using "All Fields" increases retrieval but decreases relevancy.

A good example: a researcher wanted all references to the molecule, JAK. He searched for JAK using "All Fields" and couldn't understand why he got more than 1000 references when only about a third of them discussed his molecule. It turns out that the initials, JAK, are also the three-letter code (in its own field) for the *Journal of Neural Transmission Supplement*. By using "All Fields," he retrieved articles discussing his molecule as well as every paper published in that journal.

For broadly searching by subject, use the "Text Word" field. When using this field, your terms will be searched only in the article's title, abstract, or medical subject headings (MeSH). The researcher above should have used this field. Although better than "All Fields," this approach is still likely to give you more retrieval than relevancy. The more general the search terms, the less targeted your results will be. For example, searching "ambulatory patient groups" as a text word will give you a lot of references having nothing to do with that subject.

To gain more relevancy, search your terms in the field "Title Word." This quick approach is especially productive when a few articles focusing on a topic are needed and comprehensiveness is not important. If an article has your terms in its title, you are reasonably assured that it addresses your topic.

Searching in the MeSH field is an excellent way to maximize relevancy and retrieval. PubMed uses the MeSH Browser to select the appropriate MeSH terms.

To quickly narrow a search, eliminate all foreign language articles. Select the "Language" field and enter "English." This can reduce results by as much as a third.

Narrow the search by date. The PubMed database goes back to 1966. This can greatly increase retrieval for many topics. If you are searching on a new technique or molecule, this isn't much of an issue. The easiest way to narrow by date is to use the "Entrez Date Limit" area of the current query section of the search screen. The default is "no limit." Clicking on the box reveals your choices ranging from the last 30 days to 10 years. This method can be misleading. It means you are restricting your results to the date the references were entered into the database—not the date published. Thus, selecting the last 30 days as your limit means those references retrieved were entered into PubMed within the last 30 days regardless of when the articles were published. On a related note, this is an easy way to check PubMed routinely for new references on your topic. To limit your results to a particular publication year only, select the field "Publication Date" and enter the year.

You can also limit to review articles. Select the field "Publication Type" and enter "review." Be careful not to enter the plural form "reviews."

Many clinicians are not interested in animal research, so limiting topics to human research is another trick. Select the field "MeSH Term" and enter "human." Conversely, if you are specifically looking for animal research, limit to "animal." Many articles are given both human and animal MeSH terms since both are addressed in the article. In a similar vein, limit by male or female if it is relevant to your topic. *(Ms. Anderson is Medical Librarian for the Health Sciences Library, Sequoia Health Services, Redwood City, CA.)* ❖

## CME Questions

**21. Based on the current study, which of the following is true?**
- a. Gabapentin is more effective than propranol for the treatment of essential tremor.
- b. Gabapentin is less effective than propranol for the treatment of essential tremor.
- c. Gabapentin and propranol are equally effective for the treatment of essential tremor.
- d. There is no effective treatment for essential tremor.

**22. Which of the following is associated with an increased risk for panic attacks or panic disorder?**
- a. Major depression
- b. Daily smoking
- c. Lung disease in patients who smoke daily
- d. Lung disease in patients who do not smoke daily
- e. All of the above

**23. Published data supporting the use of venlafaxine in the treatment of diabetic neuropathy include:**
- a. both case reports and double-blind studies.
- b. a single double-blind study.
- c. a case series only.

**24. Medications that may be effective for the treatment of vasovagal syncope include:**
- a. atenolol.
- b. midodrine.
- c. paroxetine.
- d. All of the above

## In Future Issues:

Vagal Nerve Stimulation for Treatment-Resistant Depression