AMERICAN HEALTH CONSULTANTS® A Medical Economics Company

PSYCHIATRIC MEDICINE IN PRIMARY CARE™

The essential guide to developments in psychiatry and behavioral health

American Health Consultants Home Page—http://www.ahcpub.com

CME for Physicians—http://www.cmeweb.com

Vagus Nerve Stimulation for Treatment-Resistant Depression

ABSTRACT & COMMENTARY

Source: Rush AJ, et al. Vagus nerve stimulation for treatment-resistant depressions: A multicenter study. *Biol Psychiatry* 2000;47:276-286.

DEPRESSION IS NOW BEING RECOGNIZED AS A CHRONIC OR RECURrent lifelong illness, rather than an isolated single episode from which lasting recovery can be expected. Although depression is most often a treatable illness, 5-15% of major depressive episodes last greater than two years and up to 1.5% of the general population suffer chronic or severe depressions. At least 10-20% of all depressed patients do not have satisfactory sustained response to present treatments.

Vagus nerve stimulation (VNS) is an approved therapy for treatment-resistant epilepsy. The current study examined the safety and potential antidepressant effects of VNS for treatment-resistant depression in an open pilot study. The idea of using VNS as a treatment for clinical depression was initially based on clinical observations of improved cognition and mood during studies of patients with epilepsy, even in subjects who did not experience improved seizure control. Further rationale for the use of VNS in the treatment of depression is provided in a companion article,[1] which notes that incoming sensory (afferent) connections of the left vagus nerve provide direct projections to many of the brain regions implicated in neuropsychiatric disorders, and that VNS has been shown to effect key neurotransmistters, including serotonin, norepinephrine, GABA, and glutamate.

In the current study, adult outpatients (n = 30) with nonpsychotic, treatment-resistant, major depression or bipolar depression, who had failed robust trials of standard treatment were implanted with the neurocyberonics prosthesis (NCP) to deliver preprogrammed stimulation to the left cervical vagus nerve (10th cranial nerve). The NCP system includes an implantable and multiprogrammable pulse generator that is surgically implanted under the skin of the chest. The generator, which delivers electrical signals to the left vagus nerve, is

INSIDE

programmed via a wand attached to a computer, much like a pacemaker.

The 12-week study included a two-week recovery period, two weeks of stimulation adjustment, and eight weeks of fixed-dose stimulation, after which patients may continue to receive longer-term follow-up and ongoing VNS treatment. Patients on antidepressant medications maintained a stable antidepressant medication regimen for at least four weeks prior to the initial baseline visit and throughout the study (medication decreases, but not increases, were allowed).

Response was defined a priori as a greater than 50% reduction in the mean Hamilton Depression Rating Scale (HRSD28) score. Of note, and appropriate to such a study, the patient population was severely ill; over their lifetimes, patients averaged 18.4 (SD = 7.3). Sixty-three percent had received electroconvulsive therapy in their lifetime. Overall, there was a 40% response rate using a greater than 50% reduction in baseline HRSD28 total score to define response.

At exit, according to the CGI-I, 3% were minimally worse, 27% were unchanged, 30% were minimally improved, 20% were much improved, and 20% were very much improved at acute phase study exit. When complete response is defined as exit HRSD28 less than 10, 17% of patients responded completely. No patient discontinued the acute study due to adverse events. Adverse events were no different than those expected from previous studies of VNS in patients with epilepsy.

COMMENT BY LAUREN B. MARANGELL, MD

This is the first report of VNS in a psychiatric population. Response rates of 40%, as well as the 17% complete response (remission) rate (exit HRSD28 less than 10), suggest efficacy in this cohort of individuals with very treatment-resistant depression. As Rush and colleagues clearly note, the small sample size and open design mandate that these data be considered preliminary. However, the chronic, disabling, and treatment-resistant nature of the depressive episodes in this patient sample make it unlikely that the response seen was unrelated to the therapeutic intervention. Given the significant number of patients that fail to respond to standard treatments, positive data for a novel intervention is remarkable, and offers hope for the many individuals who have come to believe that there is no hope for improvement. The key question will be longer-term efficacy and possibly use in other disorders that also involve brain circuits that are affected by VNS, such as obsessive compulsive disorder.[1] The use of a surgically implanted device to treat psychiatric disorders is likely to raise criticism. However, those who object to an invasive procedure to treat severe depression perhaps underestimate the suffering and disability caused by this disease. ❖

Reference

1. George MS, et al. Vagus nerve stimulation: A new tool for brain research and therapy. *Biol Psychiatry* 2000; 47:287-295.

Valproic Acid in HIV-Positive Patients: Increased Risk?

ABSTRACT & COMMENTARY

Source: Jennings HR, Romanelli F. The use of valproic acid in HIV-positive patients. *Ann Pharmacother* 1999;33:1113-1116.

THE MANAGEMENT OF PATIENTS WITH HIV DISEASE TYPIcally revolves around the suppression of HIV replication by antiviral agents such as protease inhibitors and reverse transcriptase inhibitors, as well as treatment and prophylaxis of common opportunistic infections. How-

Psychiatric Medicine in Primary Care, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.

EXECUTIVE EDITOR: Glen Harris.

MARKETING PRODUCT MANAGER: Schandale Kornegay.

ASSOCIATE MANAGING EDITOR: Robin Mason.

COPY EDITOR: Neill Larmore.

GST Registration Number: R128870672. Periodical postage pending at Atlanta, GA.

POSTMASTER: Send address changes to ***Psychiatric Medicine in Primary Care***, P.O. Box 740059, Atlanta, GA 30374.

Subscriber Information

Customer Service: 1-800-688-2421.

Customer Service E-Mail Address: customerservice@ahcpub.com

Editorial E-Mail Address: neill.larmore@medec.com

World-Wide Web: http://www.ahcpub.com

Subscription Prices

United States

$199 per year (Student/Resident rate: $100)

Multiple Copies

1-9 additional copies: $179 each. 10-20 copies: $159 each.

Outside the United States

Applicable GST plus $30 shipping

Accreditation

American Health Consultants (AHC) designates this continuing medical education (CME) activity for up to 20 hours of Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

AHC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

This CME activity was planned and produced in accordance with the ACCME Essentials.

For CME credit, add $50.

Statement of Financial Disclosure

American Health Consultants does not receive material commercial support for any of its continuing medical education publications. In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Marangell is a consultant for Pfizer, Eli Lilly, and Hoescht-Marion Roussel, is on the speaker's bureau of Wyeth-Ayerst, Eli Lilly, Abbott, Pfizer, SmithKline Beecham, BMS, Parke-Davis, and Glaxo Wellcome, and is involved in research with Pfizer, Eli Lilly, and Parke-Davis. Dr. Barber is on a speaker's bureau for Abbott. Dr. Hilty is a consultant for Pfizer, on the speaker's bureau for Pfizer, Eli Lilly, Abbott, SmithKline Beecham, and Glaxo Wellcome, and does research for Abbott. Dr. Noller and Dr. Levanthal report no relationships related to this field of study.

Questions & Comments

Please call **Robin Mason,** Associate Managing Editor, at (404) 262-5517 or **Neill Larmore,** Copy Editor, at (404) 262-5480 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

ever, HIV-positive patients are also at risk for developing neurologic manifestations such as seizures (even without a history of a seizure disorder prior to HIV infection) and psychiatric illnesses such as major depression and bipolar disorder. As a result, valproic acid (VPA) preparations (Depakote), are commonly prescribed to HIV-positive patients. There is some interesting evidence that VPA may induce the viral replication of HIV. This evidence consists of several small in vitro studies that were reviewed by Jennings and associates. The proposed mechanism for the increased viral replication by VPA relates to changes in intracellular glutathione concentrations. VPA interferes with the glutathione metabolic pathway via the inhibition of glutathione reductase. This results in decreased reduced glutathione, which provides protection against cellular oxidative damage as well as the modulation of T-cell activation. At this time, there is no conclusive evidence that the use of VPA causes increases in HIV replication in infected patients.

COMMENT BY MICHAEL F. BARBER, PharmD

Given the susceptibility of HIV-infected patients to seizures and psychiatric disorders as well as the large role of VPA in the treatment of these conditions, the possibility of increased HIV replication by VPA is important. However, no studies have shown that VPA does actually cause such increases in HIV replication in actual patients; quite often, in vitro studies do not directly translate into in vivo results. In addition, there are no studies that have looked at the ability of antiretrovirals to offset such increased viral replication as a result of lower intracellular reduced glutathione concentrations. It is clear that this area must be thoroughly evaluated before any steps toward the elimination of the use of VPA in HIV-infected individuals can be taken. These results should merely increase the awareness of clinicians and researchers to the possibility of complications in the treatment of HIV-infected patients by the use of VPA. It may be clinically warranted to pay particular attention to the viral load counts after the introduction of VPA to the profile of HIV-infected patients. If there are subsequent increases in viral load that are unaccounted for by other factors (i.e., nonadherence to the therapeutic regimen), it may be advisable to consider a change to another anticonvulsant (or mood stabilizer).

It is also important to consider other important factors that are present when adding VPA to therapeutic regimens of HIV-infected patients. First, patients with HIV disease often have hypoalbuminemia, which would result in increases in free fractions of VPA and increase the likelihood of toxicity. Second, there is an increased likelihood for pharmacokinetic and pharmacodynamic drug interactions. For instance, VPA has been shown to elicit a two- to threefold increase in cerebrospinal fluid concentrations of zidovudine. While this drug interaction may in fact increase the therapeutic efficacy of vidovudine, there may be other drug interactions that may be harmful that are as yet unreported.

The use of VPA in HIV-positive patients may have the potential for increased HIV replication. Since this finding has not been demonstrated in patients, the use of VPA should not be considered contraindicated in HIV-infected patients at this time. However, it would be prudent to keep a watchful eye on viral load counts in patients who receive VPA. ❖

To Spank or Not to Spank?

ABSTRACT & COMMENTARY

Source: MacMillan HL, et al. Slapping and spanking in childhood and its association with lifetime prevalence of psychiatric disorders in a general population sample. *CMAJ* 1999;161:805-809.

Whether to spank or not to spank children as a form of punishment in the home (and, in some parts of the country, in the school) is one of those controversial child-rearing issues about which every clinician has a strong opinion. Often this opinion is based on personal experiences—how one was raised and how one is raising (or has raised) children—as opposed to the results of scientific studies. MacMillan and colleagues used a population-based study in Ontario, Canada, to examine how often adults report that they were spanked or slapped during childhood and to determine possible relationships of this to psychiatric disorders. Similar findings have been reported from the United States.

Data for this study came from the 1990-1991 Ontario Health Supplement, a survey of 9953 residents who were at least 15 years of age. All were asked about slapping or spanking: "When you were growing up, how often did any adult slap or spank you? Often? Sometimes? Rarely? Never?" To examine the association of spanking per se with psychiatric disorders, the following respondents were excluded: Those older than 64 years of age, those who reported a history of physical abuse and/or sexual abuse, and those with missing information. A total of 4888 people were included in this part of the study. Psychiatric disorders were ascertained by a structured interview.

The majority of respondents (80%) reported that they had been slapped and/or spanked during childhood;

often, 5.5%; sometimes, 33.4%; or rarely, 40.9%. The remaining respondents (20.2%) reported never being slapped or spanked. Females reported never being slapped or spanked more frequently than males (23.9% vs 16.4%). Because of the wording of the question, it is unclear whether the spanking or slapping was by a parent or another adult.

There was a statistically significant association between the reported frequency of being slapped or spanked and anxiety, alcohol abuse or dependence, and externalizing problems such as antisocial behaviors or illicit drug abuse or dependence. An association also was noted for major depression, but the p value was 0.08.

COMMENT BY JOHN M. LEVENTHAL, MD

Here is yet another study demonstrating that physical punishment is prevalent in North America and is associated with long-term adverse outcomes in three of the four psychiatric disorders examined. A major strength of this study is the exclusion of adults who reported sexual abuse and/or physical abuse (24% of the sample) because these childhood experiences, by themselves, have been associated with psychiatric disorders. A major limitation of this study is a failure to control for other important variables in the family, such as an alcoholic parent, domestic violence, parental divorce, etc.

It is clear from this study and others that investigations on the long-term (or even short-term) consequences of spanking are methodologically difficult to conduct. Of course, the perfect study—a randomized, controlled trial of spanking—is not ethically possible, so we are left with observational studies and potential biases. In such studies, the most important bias is the failure to control for critical family variables that are likely to be associated with the occurrence of the outcome.

A second important potential bias relates to people's memories about how they were raised. For instance, in MacMillan et al's study, if respondents with alcohol-related problems over-reported the frequency of slapping or spanking, then these falsely inflated frequencies would result in a false association with the outcome of alcohol abuse or dependence.

For those who believe that spanking is not good for children, the results of this study will provide further support; for those who favor physical punishment, the limitations of the study will be noted. It is hard to imagine a study design that would convince those at the extremes. Keep in mind, however, when studies examining the short- or long-term consequences of physical punishment do find an effect, it is usually a negative effect. *(Dr. Leventhal is Professor of Pediatrics at the Yale School of Medicine, New Haven, CT.)* ❖

Quality Improvement Programs for Depression in Managed Primary Care

ABSTRACT & COMMENTARY

Source: Wells KB, et al. Impact of disseminating quality improvement programs for depression in managed primary care. *JAMA* 2000;283:212-220.

REGRETTABLY, THE QUALITY OF CARE FOR DEPRESSION in managed primary care settings is moderate to poor with resultant poor outcomes.[1] Since depression is expected to be the second leading cause of disability worldwide this century,[2] improving care for patients with depression is essential. Wells and colleages undertook the first randomized study to assess quality improvement (QI) interventions in primary care by comparing the effect of QI dissemination vs. usual care for patients with depression currently, in the past 12 months, and/or recurrent during their lifetime. Health-related quality of life and use of services were also assessed. Managed care clinics (N = 46) were grouped into clusters based on patients, demographics, clinician specialty, and distance to mental health providers. Depressed, adult, English- and Spanish-speaking patients were eligible if they had insurance. The QI intervention included: 1) an institutional commitment to pay 50% of the cost to implement to program (between $30,000-$72,000 per site for one year); 2) training of local leaders, including a primary care physician (PCP), nursing supervisor, and a mental health specialist to implement interventions—the specialist did monthly lectures and provided feedback to PCPs by monthly chart audits; 3) training of local staff-nurses provided brief clinical assessments and headed patient education via pamphlets and videos; and 4) identification of current and/or past depression by the Center for Epidemiologic Studies Depression (CES-D) scale, with clinic (intervention) or patient notification (usual care). A cut-off score of 20 on the CES-D was used to identify depression. The Short-Form 12 (SF-12) was used to track health-related quality of life. Quality of care for medications was assessed according to appropriate national guidelines. The enrolled sample included 443 usual care and 913 intervention patients. The sample had a mean age of 44 years, was 71% women, 57% non-Hispanic white, and 30% Hispanic. About 50% had depression in the past 12 months and 75% had a previous episode over their lifetime. Adherence rates for QI interventions were as follows: 100% of the psychiatrist

leaders were trained, 100% of the clinic staff were trained, 80% of PCPs attended one or more lectures, 60% of primary care physicians received feedback from expert chart audits, 73% of patients visited a nurse specialist for education and follow-up assessment of depression, and only 40% of therapy patients received cognitive-behavioral therapy. At six months, 50.9% of QI patients and 39.7% of usual care patients had counseling or used medication according to guidelines, with a similarly significant difference at 12 months (59.2% vs 50.1%). Intervention patients were about 10% less likely to be depressed and had improved health-related quality of life at six- and 12-month follow-up. For those in remission, the intervention decreased the likelihood of depression occurring by 10% in the first six months and by 19% in the second six months. In a secondary analysis, the medication subgroup had more pronounced and sustained effects than the therapy intervention. Overall, medical visits (to PCPs) did not increase for intervention patients, but these patients were also 30% more likely to have a mental health specialist visit during the study. All data analysis used an intent-to-treat analysis, and controlled for age, sex, education, and 19 chronic medical conditions.

COMMENT BY DONALD M. HILTY, MD

This is an ideal trial for the treatment of depression in primary care because of the naturalistic conditions, practical interventions, and the competence in which the study was carried out. The sample had high rates of depression over the past 12 months and overall, for lifetime episodes—this is probably due the high prevalence of depression and the duration of episodes, which are not uncommonly extended in settings without ideal treatment. Limitations include a potential bias toward worse outcomes for intervention patients because of design and analytic methods, which probably understated the benefits of the intervention. It would have also been useful to follow these patients longer, because an even greater intervention effect would be seen. Cost-effectiveness analyses are now needed for clinics to decide whether to implement such QI programs for depression and other medical disorders. Physicians in a primary care may want to consider implementation of depression QI programs. A focus on medication interventions, which are available and easier to standardize than therapy interventions, may be an appropriate first step. ❖

References

1. Wells KB, et al. Quality of care for primary care patients with depression in managed care. *Arch Fam Med* 1999;8:529-536.
2. Murray CJ, et al. The global burden of disease: A comprehensive assessment of mortality and disability From disease, injuries, and risk factors in 1990 and projected to 2020. Boston, Mass: The Harvard School of Public Health on behalf of the World Health Organization and the World Bank, 1996.

Mortality Among Recent Purchasers of Handguns

ABSTRACT & COMMENTARY

Source: Wintemute GJ, et al. Mortality among purchasers of handguns. *N Engl J Med* 1999;341:1583-1589.

DESPITE RECENT RESTRICTIONS PUT IN PLACE IN MANY states, handgun ownership remains common in the United States. More than one-fourth of all men and approximately one in 12 women own a handgun. Wintemute and colleagues used data from California in an attempt to determine whether recent legal purchasers of handguns were at increased risk for suicide or firearm death following purchase.

All persons who purchased handguns from licensed firearm dealers in California in 1991 (238,292 individuals) represent the study group. These individuals were compared to all California residents. Although Wintemute et al focused on the first few weeks and months following handgun purchase, the cohort was followed for six years.

Suicide was the leading cause of death during the initial 12 months following handgun purchases, accounting for nearly one-fourth of all of the deaths in the study group. When suicide by means of a firearm was specifically examined, it ranked second only to heart disease as a cause of death among these adult men and women.

Although male handgun purchasers had increased suicide rates compared to the general population, the rates were even more dramatically increased among female handgun purchasers. *(See Table.)*

Table

Adult Females, California, One-Year Mortality from Suicide 1991-1992

	Handgun Purchasers	CA Adult Female Population
% of Suicides by Firearm	80.0	29.7
% of all Deaths from Suicide	39.0	0.8

Modified from: Wintemute GJ, et al. *N Engl J Med* 1999;341:1583-1589.

Among women 21-44 years of age, 52% of those who died during the first year after a handgun purchase had committed suicide, and 37% had used a firearm as their method of choice. Among all California women 21-44 years old, 6.5% of those who died had committed suicide and 2.8% had done so by means of a firearm. Female purchasers of handguns were 49 times more likely to commit suicide than the general state population.

In their discussion, Wintemute et al point out that, because all handgun purchases that served as the basis of this study were legal, such purchases identified a higher socioeconomic class than all handgun owners. In addition, because felons and others with a history of violent crime are excluded from the ability to purchase handguns in California, the rates found in this study do not apply to them.

COMMENT BY KENNETH L. NOLLER, MD

Rarely have I read an article in a medical journal that has so dramatically affected me. Most studies have shown that anyone who lives in a household with a handgun is at increased risk for a violent death. Many explanations have been put forward to explain this increase but individual studies often contradict each other.

To my knowledge, this is the first large, population-based study performed in the United States that specifically looked at death rates among handgun purchasers and compared them to similar rates in the entire adult population. The results are disturbing and have great importance for those of us who provide health care to women. Although many of us have asked about "guns in the household" for years, this study suggests that it is important for us to refine the question and specifically ask about handgun purchases or planned purchases. Indeed, because so few handgun purchases are made by women, the fact that a patient has purchased or is considering the purchase of a handgun should alert us to the fact that she might be doing so to provide herself with a readily accessible method of suicide. I have always been taught that suicide by firearms was extremely rare in the female population. While it still occurs less frequently among women than among men, the fact that a woman who has purchased a handgun is 49 times more likely to die from suicide during the next year than the general female population must be acknowledged.

While there are limitations to this study (any studies dealing with state-collected statistics have severe limitations), I would strongly urge all readers to review this article. *(Dr. Noller is Chairman, Department of OB/GYN, University of Massachusetts Medical Center in Worcester.)* ❖

Melatonin for Insomnia During Benzodiazepine Discontinuation

ABSTRACT & COMMENTARY

Source: Garfinkel D, et al. Facilitation of benzodiazepine discontinuation by melatonin: A new clinical approach. *Arch Intern Med* 1999;159:2456-2460.

BENZODIAZEPINES ARE COMMONLY USED FOR TREATING insomnia but are not recommended for chronic use. However, many patients take benzodiazepines for longer than recommended periods and have problems such as rebound insomnia while discontinuing therapy. The current study investigates the use of melatonin, a hormone that promotes normal sleep in humans, to facilitate benzodiazepine discontinuation. Thirty-four subjects receiving benzodiazepine therapy were enrolled in the two-period study. In period one, patients received 2 mg of controlled-release melatonin or placebo in double-blinded fashion for six weeks. Subjects were encouraged to reduce their benzodiazepine dosage by 50% during week 2, 75% during weeks 3 and 4, and to discontinue benzodiazepine therapy completely during weeks 5 and 6. In period two, all subjects received melatonin in single-blinded fashion for six weeks and attempts to discontinue benzodiazepine therapy were resumed. Benzodiazepine use and subjective sleep-quality scores were reported daily by all patients. Subjects were then allowed to continue melatonin therapy and follow-up reassessments were performed six months later.

After period one, 14 of 18 subjects who had received melatonin therapy discontinued benzodiazepine therapy compared to four of 16 in the placebo group ($P = 0.006$). Sleep-quality scores were significantly higher in the melatonin therapy group ($P = 0.04$). Six additional subjects in the placebo group discontinued benzodiazepine therapy when given melatonin in period two. Good sleep quality was maintained in 19 of 24 patients who discontinued benzodiazepine and received melatonin therapy, as reported during the six-month follow-up. Melatonin therapy was well-tolerated by all subjects, with adverse effects being minimal and comparable in both groups (2 melatonin-treated subjects and 1 placebo-treated subject reported headaches). Garfunkel and associates concluded that controlled-release melatonin may effectively facilitate discontinuation of benzodiazepine therapy while maintaining good sleep quality.

COMMENT BY MICHAEL F. BARBER, PharmD

Many patients receive chronic benzodiazepine therapy for a variety of disorders, including anxiety disorders and sleep disorders. While the benzodiazepines are relatively safe and effective agents, their long-term use is not recommended for reasons such as tolerance and abuse potential. Thus, clinicians often may wish to discontinue the benzodiazepines in some patients. Although careful titration (i.e., reducing the total daily dose of the benzodiazepine by approximately 25-50% weekly) can help minimize such complications such as rebound anxiety and other related withdrawal symptoms, insomnia is a ubiquitous problem in patients undergoing benzodiazepine discontinuation. While some medications such as diphenhydramine and trazodone may help treat this insomnia, these agents often fail or are intolerable to some patients. Melatonin is a logical agent to evaluate for this purpose since the chronic use of benzodiazepines can suppress the endogenous release of melatonin during the normal burst hours. This may be due to a disruption of the normal sleep-wake cycle based upon circadian rhythm. Thus, the use of melatonin may actually serve to correct the disruption of the sleep-wake cycle, allowing for normal sleep patterns to continue.

This study of the use of melatonin for insomnia in patients undergoing benzodiazepine discontinuation was conducted in a relatively small number of patients; thus, the results should be considered as preliminary evidence. It is important to note that the role of melatonin in these patients is to treat insomnia, thereby facilitating benzodiazepine discontinuation. However, melatonin cannot prevent benzodiazepine withdrawal symptoms and thus does not eliminate the necessity of gradual dose reduction in patients who have been receiving benzodiazepines for an extended period of time. However, the use of melatonin may overall lead to better patient adherence to benzodiazepine discontinuation. ❖

Hypertension and Panic Attacks

ABSTRACT & COMMENTARY

Source: Davies SJ, et al. Association of panic disorder and panic attacks with hypertension. *Am J Med* 1999;107: 310-316.

TO FURTHER CHARACTERIZE THE POTENTIAL ASSOCIATION between panic disorder and hypertension, Davies and colleagues studied hypertensive family practice (HFP) patients, normotensive family practice (NFP) clinic patients, and hypertensive hospital-based clinic (HHC) patients. HFP patients were randomly sampled, with hypertension identified by a computerized problem list, antihypertensive treatment, or chart documentation of a recent blood pressure measurement of 160/90 or greater. In the same clinic, NFP patients were matched for age and gender. Finally, hypertensive patients from another clinic (HHC) were matched with the HFP patients by age and gender, excluding those (82) who were participating in a medication trial for panic disorder. All three groups were mailed a cover letter, a questionnaire based on DSM-III-R for panic attacks and panic disorder, a Hospital Anxiety and Depression Scale, and supplementary questions on medications and age at diagnosis of hypertension. Those not responding within two months were sent another questionnaire; they were deemed nonresponders if they had not replied within six weeks.

Of the 1053 questionnaires sent, 916 (88%) were returned; 25 were excluded because of uninterpretable responses or having been miscategorized (e.g., hypertensive instead of normotensive). HFP and HHC patients had a significantly greater prevalence of lifetime and current panic attacks than the NFP patients; only HFP had a significantly greater prevalence of panic disorder diagnosis *(see Table)*. Anxiety scores were significantly higher in the HPC and the HHC groups compared to the NFP group; only HHC patients had significantly higher depressive scores compared to NFP patients. As for the effect of gender, both men and women with hypertension had elevated rates of panic attacks. Prevalence of panic symptoms was not related to age. Hypertensive patients who had experienced panic attacks (n = 197) were asked their ages at the time of the first panic attack and at diagnosis of hypertension. Hypertension preceded panic attacks in 48%, panic attacks preceded hypertension in 27%, and the timing coincided for 25%. There were no differences in antihypertensive use in those with and without panic symptoms.

Table

Prevalence of Lifetime and Current Panic Attacks and the Diagnosis of Panic Disorder

Issue	HFP	NFP	HHC
Lifetime prevalence of panic attacks	35%*	22%	39%*
Prevalence of current panic attacks	17%*	11%	19%*
Diagnosis of panic disorder	13%*	8%	10%

*Signifies P < 0.05 compared to NFP patients.

Davies et al considered several possible reasons

why panic symptoms and hypertension may be associated. First, panic symptoms could increase the chance of hypertension being diagnosed through greater medical contact. Second, antihypertensive medication may be initiated due to elevations in blood pressure associated with panic attacks and/or hyperventilation rather than hypertension. Finally, hypertension and panic attacks might be linked by a shared etiology (e.g., pheochromocytoma).

COMMENT BY DONALD M. HILTY, MD

The apparent association of panic disorder and hypertension is noteworthy. However, this study does not allow an examination of a causal or non-causal relationship; it looks at the prevalence of panic attacks and panic disorder in patients with and without hypertension. In addition, there are several important methodological limitations to this study. Self-administered questionnaires are practical but less valid than clinical diagnoses. The study did not control for comorbid medical conditions that may influence the prevalence of panic attacks (e.g., smoking, depression, lung disease—see Hilty DM. Are smoking and panic attacks related? *Psychiatr Med Prim Care* 2000;1:92-93.) By increasing the risk for cardiac disease, hypertension might indirectly increase the risk for panic attacks (cardiac disease was not assessed as a confounding variable). Similarly, norepinephrine may be involved in both panic attacks and hypertension. Finally, 82 patients in the HHC group were excluded because they participated in a prior panic study—this in all likelihood artificially lowered the prevalence rates for panic attacks and panic disorder in that group. ❖

CME Questions

1. **Which of the following statements about vagus nerve stimulation (VNS) are *false*?**
   a. VNS is an approved therapy for treatment-resistant epilepsy.
   b. VNS requires a minor surgical procedure to implant the generator and lead.
   c. VNS has shown promising results in an initial pilot study of patients with treatment-resistant depression.
   d. VNS is clearly effective in a variety of psychiatric disorders.

2. **Which of the following is *false*?**
   a. Panic attacks occur in a greater number of hypertensive patients than normotensive patients.
   b. Panic disorder occurs in a greater number of hypertensive patients than normotensive patients.
   c. Other medical problems that increase the likelihood of panic attacks include smoking, depression, and lung disease.
   d. Hypertension has a causal relationship with panic disorder.
   e. Patients with any anxiety disorder may be more likely to have hypertension.

3. **Valproic acid may have the potential for increased HIV replication, but this finding has not been demonstrated in patients. As such, the use of valproic acid is not contraindicated in HIV-infected patients, but it may be prudent to keep a watchful eye on viral load counts in such patients who receive VPA.**
   a. True
   b. False

4. **A woman who has purchased a handgun is 49 times more likely to die from suicide during the next year than the general female population.**
   a. True
   b. False

In Future Issues:

Irritable Bowel Syndrome: New Pharmaceutical Approaches to Treatment