AMERICAN HEALTH CONSULTANTS®

# NEUROLOGY ALERT®

Providing Evidence-based Clinical Information for 21 Years

*A monthly survey of developments in neurologic medicine*

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

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



## Another Drug for the Migraine Prophylaxis Armamentarium

ABSTRACT & COMMENTARY

**Source:** Tronvik E, et al. Prophylactic treatment of migraine with an angiotensin II receptor blocker. *JAMA*. 2003;289:65-69.

SEVERAL LINES OF EVIDENCE SUGGEST THAT ACE INHIBITION and/or angiotensin receptor blockade can be effective for migraine prevention. Lisinopril has already been shown to reduce migraine headache.[1] However, the excellent side-effect profile of the angiotensin receptor blockers (ARB) make them better candidates for this indication as these patients are either otherwise young and healthy and do not want drugs with side effects or they are already on many drugs and do not need any additional problems. Tronvik and colleagues report on the first well-designed trial of an ARB—candesartan for migraine prevention.

Sixty IHS-defined migraine patients aged 18-65 with 2-6 migraine attacks per month were enrolled in a randomized, double-blind, placebo-controlled crossover single-center study. A placebo run-in period of 4 weeks was followed by 2 12-week treatment periods separated by 4 weeks of placebo washout. Thirty patients were randomized in each group to receive 16 mg of candesartan or placebo once per day. The primary end point was "the number of days with headache." In the ITT analysis (n = 57) for the 12-week period, the mean number of days with headache was 13.6 with candesartan vs 18.5 in the placebo group ($P = 0.001$). Most of the secondary end points also favored the candesartan group, such as days with migraine (12.6 vs 9.0; $P < .001$), headache severity index (293 vs 191; $P < .001$), and disability level (20.6 vs 14.1; $P < .001$). There was no difference between either group with respect to quality of life as measured on the Short Form 36 questionnaire. For each efficacy outcome, a "responder" was recorded when a symptom reduction of at least 50% was observed in the treatment group compared to placebo in accordance with IHS guidelines. As such in the candesartan group 18/57 (31.6%) had a > 50% reduction in "days with headache" and 23/57 (40.4%) for "days with migraine" compared to 1/57 (1.8%) and 2/57 (3.5%) in the placebo group ($P = .001$). Adverse events were similar in both groups.



VOLUME 21 • NUMBER 7 • MARCH 2003 • PAGES 49-56

## COMMENTARY

Aside from the small study size, several positive points can be made. First, the candesartan responder rates for headache and migraine days compares favorably with the published outcomes for several of the established migraine prophylactic drugs, such as propranolol and valproate, which are within the 30-40% range. Second, the small sample size most likely accounts for inability to demonstrate an advantage on quality-of-life measures in the candesartan group. Third, the lack of adverse effects and the overwhelming high tolerance of candesartan makes not only this drug but the whole class of ARBs a compelling new option for migraine prophylaxis. There is no effect on hemodynamics, no sexual dysfunction, no anticholinergic effects, no weight gain, nor is there a contraindication to asthma or diabetes, to name just a few of the advantages. One can only speculate as to the mechanism of action. Tronvik et al suggest several possibilities, including direct vasoconstriction, increased sympathetic discharge, and actions on angiotensin type I receptors within the brain itself. But virtually all of the present-day migraine preventatives lack an understanding of mechanism, and instead, we rely on the empiric evidence such as we have.

**— JEFFREY REICH**


***Neurology Alert,*** ISSN 0741-4234, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

**VICE PRESIDENT/**
**GROUP PUBLISHER:** Brenda Mooney.
**EDITORIAL GROUP HEAD:** Glen Harris.
**MANAGING EDITOR:** Robin Mason.
**ASSISTANT MANAGING EDITOR:** Robert Kimball.
**SENIOR COPY EDITOR:** Christie Messina.
**MARKETING PRODUCT MANAGER:** Schandale Kornegay.
**GST Registration Number:** R128870672.
Periodicals postage paid at Atlanta, GA.
**POSTMASTER:** Send address changes to ***Neurology Alert,*** P.O. Box 740059, Atlanta, GA 30374.




**Back issues: $40.** Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.


**Subscriber Information**

**Customer Service: 1-800-688-2421.**
**Customer Service E-Mail Address:**
customerservice@ahcpub.com
**Editorial E-Mail Address:** christie.messina@ahcpub.com
**World-Wide Web:** http://www.ahcpub.com

**Subscription Prices**

**United States**
1 year *with* free AMA Category 1 credits: $287
Student/Resident rate: $145
**Multiple Copies**
2-9 additional copies: $213. 10-20 copies: $190.
**Canada**
Add 7% GST and $30 shipping.
**Elsewhere**
Add $30 shipping.

**Accreditation**

American Health Consultants (AHC) designates this educational activity for a maximum of 25 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.
Each physician should claim only those hours of credit that he/she actually spent in the educational activity.
This CME activity was planned and produced in accordance with the ACCME Essentials.
AHC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

THOMSON
AMERICAN HEALTH CONSULTANTS

**Questions & Comments**

Please call **Christie Messina**, Senior Copy Editor, at (404) 262-5416 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.


### Statement of Financial Disclosure

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. Apatoff is on the speaker's bureau of Biogen and Teva. Dr. Relkin is on the speaker's bureau of Pfizer, Eisai, and Athena Diagnostics and does research for Pfizer and Merck. Dr. Rubin does research for ASTA Medica and Eli Lilly. Dr. Beal is a consultant for Mitokor and Avicena. Dr. Segal is on the speaker's bureau of Boehringer-Ingelheim. Dr. Plum, Dr. Frucht, Dr. Lado, Dr. Reich, and Dr. Trifiletti report no consultant, stockholder, speaker's bureau, research, or other relationships related to this field of study.

### Reference


1. Schrader H, et al. *BMJ*. 2001;322:19-22.


# A New Benign Sexual Headache: Sildenafil (Viagra®)-Induced Migraine

ABSTRACT & COMMENTARY

**Source:** Kruuse C, et al. Migraine can be induced by sildenafil without changes in middle cerebral artery diameter. *Brain*. 2003;126:241-247.

According to the PDR,[1] 16% of patients using sildenafil in clinical trials reported headache compared with only 4% of controls. Kruuse and associates studied the effect of sildenafil use apart from sexual activity in 12 patients with a history of migraine without an aura. In a double-blind, placebo-controlled crossover study, sildenafil 100 mg or placebo was administered orally on 2 separate days. Middle cerebral artery blood flow velocity (Vmca) was recorded by transcranial Doppler ultrasonography, and regional cerebral blood flow (rCBF) was measured using SPECT and Xenon133 inhalation.

Migraine attacks were induced by sildenafil in 10/12 migraine patients and by placebo in 2 of 12 ($P = 0.01$). Sildenafil did not affect Vmca, rCBF, temporal or radial artery diameter, tenderness of pericranial vessels, or blood pressure. Heart rate increased significantly from a mean of 62 ± 2 before to 74 ± 3 beats/min after sildenafil ($P = 0.01$).

Sildenafil is a selective inhibitor of the cyclic guanosine monophosphate (cGMP)-degrading enzyme phosphodiesterase 5 (PDE5). PDE5 is located in several different sites throughout the body, including the vascular smooth muscle of the penis where it regulates vascular tone. The effects of sildenafil on cerebral artery tone are unknown.

In the present study, migraine headaches induced by sildenafil occurred without an initial dilatation of the MCA. Therefore, Kruuse et al postulate that a sildenafil-induced increase in cGMP may affect headache-triggering mechanisms within perivascular sensory nerve terminals, the brainstem, or at other sites.

## COMMENTARY

In the popular mind, the best-known association between headache and sexual activity is that the former

is used as an excuse to avoid the latter. Neurologists, however, recognize the role of sexual activity as a precipitant of headache and term as coital or orgasmic cephalgia benign headaches occurring at orgasm and rapidly subsiding thereafter.

In the present study, Kruuse et al found that sildenafil apart from any sexual activity induced headaches in 80% of migraine patients. It is not known whether sildenafil together with sexual activity also provokes orgasmic cephalgia and other forms of benign sexual headaches. So far, patient reporting suggests that this is not the case.

Nevertheless, this paper should remind clinicians to inquire about sildenafil use in patients reporting headaches, especially those related to sexual activity, and also to inform patients with a history of migraine headaches who plan to use sildenafil of the risk of migraine attacks. **— JOHN J. CARONNA**

### Reference

1. *Physicians' Desk Reference*. 57th ed. Montvale, NJ: Medical Economics Company Inc; 2003:2656.

## Rasagiline in Early Parkinson's Disease

ABSTRACT & COMMENTARY

**Source:** The Parkinson Study Group. A controlled trial of rasagiline in early Parkinson Disease. *Arch Neurol*. 2002;59: 1937-1943.

Like its cousin selegiline, rasagiline is a selective irreversible inhibitor of monoamine oxidase type B. Rasagiline has been shown to improve the motor and cognitive signs of experimental parkinsonism, and preliminary studies have demonstrated that the compound is more potent than selegiline. A prior study of rasagiline in early Parkinson's disease demonstrated that the drug was well tolerated up to doses of 4 mg/d. The theoretical risk of severe hypertensive crisis from nonselective inhibition of monoamine oxidase (seen with the older antidepressants Parnate and Nardil) was not observed.

Members of the Parkinson Study Group embarked on a double-blind, parallel-group, randomized, placebo-controlled trial of rasagiline in patients with early Parkinson's disease in 1997. This trial randomized patients to receive placebo, 1 mg/d, or 2 mg/d of drug for a period of 26 weeks, after which the drug was withdrawn. Only patients afflicted with early Parkinson's disease who did not require treatment with levodopa or dopamine agonists were allowed to enroll. They also could not have evidence of depression or dementia and were required to be in good health. The primary end point of the study was the change in total score of the Unified Parkinson Disease Rating Scale, a statistically validated clinical rating scale.

A total of 404 patients were enrolled in the trial—138 to placebo, 134 to 1 mg of drug, and 132 to 2 mg of drug. Of these, 112, 111, and 105 patients completed the 26-week trial, respectively. Both active groups showed a statistically significant benefit in the clinical rating score relative to placebo. However, the improvements were small and, in fact, were slightly better for the 1-mg than the 2-mg group. There was no difference in the rate of minor adverse events between the groups. However, 20 serious adverse events occurred during the study—4 in the placebo group, 6 in the 1-mg group, and 10 in the 2-mg group. This included 3 patients in the 2-mg group newly diagnosed with malignancies (malignant melanoma, prostate carcinoma, and squamous cell carcinoma of the skin). There was also a small but statistically significant (4 mm Hg) rise in supine systolic blood pressure in the 2-mg group relative to placebo.

### COMMENTARY

Several lessons can be learned from this well-designed, carefully performed study. First, rasagiline was well tolerated, and most patients were able to complete the study. There was no evidence that the 2-mg dose was superior to the 1-mg dose. The improvements in rating scale scores were similar to results observed in the DATATOP trial of selegiline. Compared to the robust improvement in scores seen in trials of dopamine agonist monotherapy in early Parkinson's disease, these rating scale improvements are modest.

The incidence of adverse events was higher in the active treatment arms, particularly the 2-mg group. The development of 3 new malignancies (including 1 case of melanoma) in this group raises concerns; however, the sample size and duration of treatment are too short to draw definitive conclusions about the safety of the drug. While rasagiline likely produces its clinical effect by extending the life of endogenous dopamine, the possibility exists that the drug may be neuroprotective. Further larger and longer trials of this agent in Parkinson's disease are in progress. **— STEVEN FRUCHT**

# New Practice Parameters for Treatment of Seizures

ABSTRACTS & COMMENTARY

**Sources:** Chang BS, Lowenstein DH. Antiepileptic drug prophylaxis in severe traumatic brain injury. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2003;60:10-16; Hirtz D, et al. Treatment of the child with a first unprovoked seizure. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2003;60:166-175.

PRACTICE PARAMETERS FROM THE AAN "ARE STRATEgies for patient management that assist physicians in clinical decision-making." These recommendations are derived from a thorough review that not only summarizes the available evidence-based medicine but, more importantly, assesses the quality of the data being reviewed.

Severe head traumatic brain injury (TBI) involves loss of consciousness or amnesia for 12-24 hours, intracranial hematoma, depressed skull fracture and/or brain contusion. About 10-12% of patients with severe TBI will develop seizures. Arbitrarily, these posttraumatic seizures are defined as "early" if they occur within 7 days of the injury or "late" if they occur thereafter. Chang and Lowenstein conclude that "prophylaxis with phenytoin in patients with severe TBI is established as effective in decreasing the risk of early posttraumatic seizures." By contrast, "prophylaxis with phenytoin, carbamazepine, or valproate . . . is probably not effective in decreasing the risk of late posttraumatic seizures."

Hirtz and associates raise the question of whether it is appropriate to treat children and adolescents who have experienced a first seizure with antiepepileptic drugs (AED). They recommend that "treatment with AED is not indicated for the prevention of the development of epilepsy," but "treatment with AED may be considered in circumstances where the benefits of reducing the risk of a second seizure outweigh the risks of pharmacologic and psychosocial side effects." Neither recommendation meets the standard of being supported by a convincing Class I study.

## COMMENTARY

While it is useful to have common clinical practice codified in such a systematic way, these 2 practice parameters leave us with the disheartening conclusion that there is nothing new under the sun regarding seizure prophylaxis. We know that AEDs are effective at suppressing seizures. We also know that their effectiveness comes with the risk of untoward side effects. But, what are the mechanisms underlying epileptogenesis, and can we develop therapies to interfere with this process? This is really the issue common to treating TBI and unprovoked childhood seizures.

Recommendations for future research should be even more prescriptive than the present practice recommendations. It would be of great interest to conduct prospective, randomized, controlled trials of the newer AEDs. Trials could include topiramate and zonisamide (which are reported to have neuroprotective properties) or levetiracetam (which is supposed to suppress kindling models of epileptogenesis). The goal of the study would be to prevent the development of late posttraumatic seizures or epilepsy in children following a first unprovoked seizure. Such studies offer the promise of important future revisions of the current practice parameters.

**— ANDY DEAN**

*Dr. Dean is Assistant Professor of Neurology and Neuroscience, Director of the Epilepsy Monitoring Unit, Department of Neurology, New York Presbyterian Hospital—Cornell Campus.*

# A Look at Some Memorable Brains

ABSTRACT & COMMENTARY

**Source:** Maguire EA, et al. Routes to remembering: The brains behind superior memory. *Nat Neurosci*. 2003;6(1):90-95.

DISORDERS OF MEMORY ARE FREQUENTLY STUDIED, but exceptional recall abilities have been the subject of relatively few investigations. In an effort to understand the neural basis of superior recall, Maguire and associates examined 8 participants in the World Memory Championships, a competition held annually in London. These individuals averaged nearly 34 years of age and had practiced the use of memory-enhancing strategies (mnemonics) for an average of 11 years. Most used an ancient mnemonic strategy known as the "Method of Loci," in which the items to be recalled are associated with a well-learned route or other mentally visualized locations. Maguire et al used neuropsychological testing, quantitative analysis of MRIs by voxel-based morphometry, and functional MRI (fMRI) to

compare the superior memorizers (SM) to age-matched normal controls.

The performance of the SM and controls on the neuropsychological test was similar in terms of verbal IQ, reasoning ability, and visual recall. However, there were differences observed in the ability to repeat random sequences of digits (digit span). The SM were able to repeat an average of 16.8 digits presented orally, while controls scored only 12 digits forward. In addition, performance on measures of verbal memory, such as the Story Recall Test and the Subjective Memory Questionnaire, also favored the SM over those with normal memory abilities.

The gross structure of the brains of the SM did not differ significantly from that of controls. The fMRI studies, however, did reveal differences. The tasks used in the fMRI studied included recall of digits, faces, and the patterns in drawings of snowflakes. The SM were better at memorizing things that could be more readily described verbally, such as digits and faces, but they were not better than controls at recalling stimuli that could not readily be verbally encoded, such as the random patterns of snowflakes. Across fMRI tasks, the SM more extensively activated the right hippocampus, the medial parietal cortex, and the retrosplenial cortex than did their age-matched counterparts. These regions of the brain are known to be important for certain aspects of memory, especially spatial memory and navigation. Maguire et al suggest that the greater activation of these areas in the brains of the SM relates to their use of the Method of Loci to improve their recall performance. They conclude that fMRI may be useful in future studies of the neural basis of mnemonic strategies.

### COMMENTARY

It would be of great value to understand how some individuals develop exceptional recall abilities. That knowledge might lead to improved strategies for education, methods to preserve recall in the elderly, or techniques to remediate memory loss in patients with certain neurologic disorders. This investigation of SM provides some interesting insights into exceptional memory performance and suggests the value of applying mnemonics for memorization enhancement.

It is notable that the SM in this study were not better at recalling visual patterns than the age-matched controls. They apparently did not have eidetic recall (photographic memory), the ability to remember scenes in comparable detail to examining a photograph. There is no evidence that true eidetic recall can be learned or acquired through the use of any known mnemonic strategies. Verbal recall abilities, however, can be enhanced through techniques such as the Method of Loci, which has been used successfully for this purpose for more than 2000 years. This fMRI study provides evidence that brain areas specialized for spatial recall are recruited when the Method of Loci is used. In terms of clinical benefit from the use of this mnemonic strategy, it seems likely that this strategy would succeed only in patients in whom these brain regions remain intact. Considerable effort is required to successfully learn and apply this mnemonic technique in a real-world setting, and it is, therefore, useful to know which patients it would or would not benefit.

As Maguire et al suggest, fMRI may be a valuable tool with which to examine the neural underpinnings of mnemonics. In addition, fMRI could prove useful in matching particular individuals with the mnemonic strategies that are best suited for them to learn.
**— NORMAN R. RELKIN**

# Demyelinating Neuropathy and Antineurofilament Antibodies

ABSTRACT & COMMENTARY

**Source:** Stubbs EB Jr, et al. Anti-neurofilament antibodies in neuropathy with monoclonal gammopathy of undetermined significance produce experimental motor nerve conduction block. *Acta Neuropathol*. 2003;105:109-116.

Among patients with plasma cell dyscrasias and polyneuropathy, most have monoclonal gammopathy of undetermined significance (MGUS), of which 50% are IgM in type. Most of these demonstrate activity against myelin-associated glycoprotein (MAG). Other IgM antibodies are reactive against acidic glycolipids, GM1 and GD1b gangliosides, intermediate filaments, chondroitin sulfate C, sulfatide, and neurofilament. Segmental demyelination is seen with most of these, but chondroitin sulfate C, sulfatide, and neurofilament demonstrate axonal degeneration. Although it is tempting to attribute the neuropathy to the antibody, a definite cause-and-effect relationship has yet to be established for any of the associations, though it is strongest for anti-MAG demyelinating polyneuropathy.

Sixteen patients presenting with distal symmetric polyneuropathy and preserved strength had IgG MGUS on laboratory evaluation. All had normal serum IgM and IgA levels, normal bone marrow biopsy, and absence of diabetes, toxin exposure, Bence-Jones proteinuria, lytic

bone lesions, anemia, hypercalcemia, amyloidosis, organomegaly, or renal insufficiency. Four of the 16 patients' sera contained elevated polyclonal IgG antibodies. On immunoblot, the IgG reacted with a high molecular mass protein which, when sequenced, was confirmed to be high-molecular-weight neurofilament (NFH) protein. Demyelinating neuropathy was seen on nerve conduction studies in 2 of the 4 patients, with an axonal and a mixed axonal-demyelinating neuropathy in 1 each. None of 10 control sera demonstrated these antibody activities and the 4 patients' own IgG monoclonal antibodies were nonreactive as well. When NFH was injected into rat sciatic nerve endoneurium together with complement-supplemented sera, motor nerve conduction block was documented electrophysiologically with no evidence of temporal dispersion. Injection of NFH alone, without complement-supplemented sera, failed to produce conduction block. Injection of complement-supplemented sera alone was similarly nonpathogenic. Pathologic study of the NFH-complement injected nerve revealed axonal shrinkage, with myelin vesiculation, ovoid formation, and edema. Polyclonal NFH antibody activity may be causally related to IgG MGUS demyelinating neuropathy.

### COMMENTARY

Polyclonal antibodies are nonpathogenic.[1] Association between IgG or IgA MGUS and polyneuropathy is tenuous. Hence, this report is doubly intriguing and raises several questions. Patients demonstrated normal strength, indicating an absence of significant conduction block, yet the rat model showed evidence of just such pathology. Nerve conduction results were similarly predominantly demyelinating, but whether they involved motor or sensory nerves, or both, remained unstated. Numbers were small (n = 4) and 1 patient with a mixed axonal-demyelinating neuropathy "developed a smoldering multiple myeloma." Confirmation of these results in other, larger, series will be desirable to confirm or contradict its findings. **— MICHAEL RUBIN**

### Reference

1. Gorson KC, et al. *Neurology*. 1997;49:1747.

## A Fishy Story About Stroke

ABSTRACT & COMMENTARY

**Source:** He K, et al. Fish consumption and risk of stroke in men. *JAMA*. 2002;288:3130-3136.

Several previous studies have reported inverse associations between fish intake and the risk of stroke in men[1] and women.[2] A randomized trial in patients with coronary heart disease, however, found that supplementation with fish oil reduced the risk of acute myocardial infarction but not of stroke.[3] Therefore, He and associates prospectively examined the relation between fish intake and risk of stroke in a large cohort of male health professionals who completed dietary measurements in 1986-1998. More than 43,000 men aged 40-75 without diabetes mellitus or symptomatic vascular disease (cerebral, cardiac, or peripheral) at baseline were followed. Fish consumption was computed as the sum of frequency of intake as a main dish of 4 different items: canned tuna fish; dark meat fish such as salmon, swordfish, sardines, etc; other fish; and shrimp, lobster, or scallops. Participants also were asked about the use of fish oil and vitamin supplements and the use of aspirin or antiplatelet agents.

There were 608 strokes during the 12 years of follow-up, including 377 ischemic, 106 hemorrhagic, and 125 unclassified strokes. Compared with men who consumed fish less than once a month, the multivariate relative risk (RR) of ischemic stroke was lower among those who ate fish 1-3 times per month (RR, 0.57; 95% confidence interval [CI], 0.35-0.95). The inverse association between fish intake and risk of ischemic stroke was not modified by the use of aspirin. A higher frequency of fish intake (> once per week) was not associated with further risk reduction. There was no significant association between fish or long-chain omega-3 polyunsaturated fatty acids intake and hemorrhagic stroke; however, the relatively small number of cases means that the possibility that high fish consumption increases risk of hemorrhagic stroke cannot be ruled out.

### COMMENTARY

He et al found that even low fish consumption, at least once a month, was associated with significantly lower risk of ischemic stroke. As they themselves noted, the "biological mechanism of the apparent beneficial effects of such a small amount of fish intake and the lack of a dose response remain unclear." Before we accept these results as proof of the homeopathic method of treating diseases with very small doses of drugs, we should recall as someone wisely said, "Food is never just something to eat." Eating fish frequently may be an indicator of a lifestyle that reduces stroke risk. In fact, He et al reported that men with high fish consumption were less likely to be current smokers or overweight and more likely to be physically active and to use aspirin or multivitamin supplements. They were also more likely to have a history of hypertension and hypercholesterolemia.

Clinicians must continue to interpret recent scientific and unscientific reports linking certain diets and disease prevention. Patients who seek dietary shortcuts to health and fitness must be counseled concerning the role of diet along with medications and physical activity in achieving well-being. An apple a day, a glass of red wine every week, and a tuna fish sandwich every month may all be good but by themselves are unlikely to prevent stroke.
**— JOHN J. CARONNA**

### References


1. Keli SO, et al. *Stroke*. 1994;25:328-332.
2. Iso H, et al. *JAMA*. 2001;285:304-312.
3. GISSI-Prevenzione Investigators. *Lancet*. 1999;354: 447-455.


# Muscle-Nerve Root Correlation for EMG

ABSTRACT & COMMENTARY

**Source:** Tsao BE, et al. Comparison of surgical and electrodiagnostic findings in single root lumbosacral radiculopathies. *Muscle Nerve*. 2003;27:60-64.

Retrospective review of needle EMG findings on 45 patients studied during a 20-year period, with surgically verified compression of a single lumbosacral nerve root, was undertaken to determine the accuracy of traditional myotomal charts used to localize nerve root involvement. Only patients with preoperative neuroimaging were included. Patients with underlying polyneuropathy, previous surgery, surgical evidence of polyradiculopathy, or spinal stenosis were excluded. Muscles were classified as abnormal only if they demonstrated sustained fibrillation potentials on EMG. Muscles with polyphasic motor unit potentials without fibrillation potentials were not included (*see Table 1*).

**Table 1**

| L2 (n = 1) | L3 (n = 1) | L4 (n = 5) | L5 (n = 26) | S1 (n = 12) |
|---|---|---|---|---|
| AL | AL | AL (5) | PL (16/16) | BFLH (5/5) |
| iliacus | iliacus | iliacus (3/5) | TFL (4/4) | LG (10/11) |
| VL | VM | VL (4/5) | TP (23/25) | BFSH (8/9) |
| upper LPS | upper LPS | RF (3/3) | EDB (20/24) | MG (10/12) |
| | | VM(1/1) | TA (20/26) | ADQ (5/7) |
| | | LPS(4/5) | EHL (8/11) | GM (7/11) |
| | | | LPS (12/26) | LSPS (3/12) |

ADQ = abductor digiti quinti; AL = adductor longus; BFLH = biceps femoris long head; BFSH = biceps femoris short head; EHL = extensor hallucis longus; GM = gluteus maximus; LG = lateral gastrocnemius; LPS = lumbar paraspinal muscles; LSPS = lumbosacral paraspinal muscles; MG = medial gastrocnemius; PL = peroneus longus; RF = rectus femoris; TA = tibialis anterior; TFL = tensor fascia lata; TP = tibialis posterior; VL = vastus lateralis; VM = vastus medialis

**Table 2**

| C5 (n = 7) | C6 (n = 9) | C7 (n = 28) | C8 (n = 6) |
|---|---|---|---|
| IS (5/6) | PT (7/9) | PT (17/28) | EIP (6/6) |
| Belt (6/7) | TB (5/9) | TB (28/28) | FDI (6/6) |
| BR (5/6) | IS (3/7) | PS (8/26) | ADM (6/6) |
| BB (5/7) | Delt (3/8) | FCR (25/27) | PS (4/5) |
| PS (5/7) | BR (5/7) | RF (3/3) | |
| | FCR (4/5) | VM(1/1) | |
| | PS (5/8) | LPS (4/5) | |
| | BB (4/9) | LPS (12/26) | |

ADM = abductor digiti minimi; BB = biceps brachii; BR = brachioradialis; Delt = deltoid; EIP = extensor indicis proprius; FDI = first dorsal interosseous; FCR = flexor carpi radialis; IS = infraspinatus; PS = paraspinals; PT = pronator teres; TB = triceps brachii

Interestingly, L5 radiculopathy demonstrated normal biceps femoris short head in 13/13 examined, and S1 radiculopathy revealed normal semitendinosus and extensor digitorum brevis in all examined. Tibialis posterior is predominantly L5 innervated and was positive in only 2/11 with S1 radiculopathy. Medial and lateral gastrocnemii are predominantly S1 muscles, being positive in only 1/24 and 2/16, respectively, with L5 radiculopathy. Paraspinals were often unhelpful in L5 and S1 radiculopathy (12/26 and 3/12 positive, respectively) but were positive in the few with L2, 3, or 4 disease. Although the numbers are relatively small, pattern recognition allows many lumbosacral radiculopathies to be localized to a single level electrodiagnostically.

## COMMENTARY

Cervical radiculopathy was similarly examined among 50 surgically proven single-root lesions.[1] Patients with multiple radiculopathies, myelopathy, or previous surgery were excluded. Muscles were considered abnormal only if fibrillation potentials were documented in at least 3 sites in any given muscle, and EMG was performed a mean of 3.5 months after symptom onset in 46 patients in whom onset could be clearly defined (*see Table 2*).

Extensor digitorum communis was rarely positive in C7 (3/17) or C6 (1/5). Paraspinals were usually positive except in C7 (8/26). Because of overlap, C6 mimicked C5 as often as it did C7, and these levels may be difficult to limit to a single root electrodiagnostically.
**— MICHAEL RUBIN**

**Reference**

1. Levin KH, et al. *Neurology*. 1996;46:1022-1025.

## CME Questions

*Effective with this issue,* Neurology Alert *is changing its testing procedure. You will no longer need to return a Scantron answer sheet to earn credit for the activity. Please review the text, answer the following questions, check your answers against the key on the following page, and then review the materials again regarding any questions answered incorrectly.* ***To receive credit for this activity, you must return a CE/CME evaluation at the end of the testing term.*** *For further information, refer to the "CE/CME Instructions" below.*

*This testing procedure has proven to be an effective learning tool for adults. If you have any questions about the new testing method, please contact Customer Service at 1-800-688-2421.*

**5. Compared to those with normal memory, individuals with superior memorizing ability:**
   a. have superior verbal IQs.
   b. have unique features of brain anatomy.
   c. must possess eidetic recall abilities (photographic memory).
   d. more commonly use mnemonic strategies.

**6. Which of the following statements is *false*? Sildenafil produces headaches:**
   a. in 16% of normal subjects.
   b. in 80% of migraine subjects.
   c. by dilating cerebral vessels.
   d. by raising blood pressure.
   e. by an as yet unknown mechanism.

**7. Choose the correct statement.**
   a. Among patients with plasma cell dyscrasias and polyneuropathy, most have multiple myeloma.
   b. Among patients with polyneuropathy and monoclonal gammopathy of undetermined significance (MGUS), most are IgG in type.
   c. Among patients with polyneuropathy and monoclonal gammopathy of undetermined significance (MGUS), most demonstrate activity against myelin-associated glycoprotein (MAG).
   d. In patients with plasma cell dyscrasias and polyneuropathy, segmental demyelination is seen exclusively.

**8. The lowest frequency of fish consumption that maximally reduces ischemic stroke risk is:**
   a. < 1 per month.
   b. 1-3 per month.
   c. 1 per week.
   d. 2-4 per week.

**9. Choose the correct statement.**
   a. Extensor digitorum communis is rarely positive on EMG in C7 radiculopathy.
   b. Biceps femoris short head is usually normal on EMG in L5 radiculopathy.
   c. Semitendinosus is usually normal on EMG in S1 radiculopathy.
   d. Tibialis posterior is a predominantly L5 innervated muscle.
   e. All the above

**Answers:** 5(d); 6(c); 7(c); 8(b); 9(e)

## CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. **At the end of the testing period, you must complete the evaluation form provided and return it in the reply envelope provided in order to receive a certificate of completion.** When your evaluation is received, a certificate will be mailed to you.

## Correction

In the February 2003 *Neurology Alert*, CME question number 5 referred to an article not yet published. The article and the CME question are published in this issue. We regret any confusion this may have caused. ■

## Readers are Invited

Readers are invited to submit questions or comments on material seen in or relevant to *Neurology Alert*. Send your questions to: Christie Messina—Reader Questions, *Neurology Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. ■

**In Future Issues:** **Parkinson's Disease**

PHARMACOLOGY WATCH

# Smallpox Vaccination Guidelines Published by CDC

The CDC published "Smallpox Vaccination and Adverse Reactions—Guidance for Clinicians" in the Jan. 24th edition of *Morbidity and Mortality Weekly Report.* The guidance is a thorough review of the smallpox vaccine with a well-illustrated compendium of complications. Some of the highlights include:

Inoculation is administered using a multiple-puncture technique with the bifurcated needle. The inoculation site progresses from papule to vesicle, eventually becoming a pustule within 10 days. The pustule scabs over within 2-3 weeks usually leaving a pitted scar. Development of a pustular lesion is considered a major reaction and a successful vaccine take. Lesser reactions are considered equivocal and are nontakes. Large vaccination reactions may occur in 10% of first-time vaccinees. Systemic reactions are common in all vaccinees and include fatigue, headache, myalgias, chills, nausea, and fever. The vaccine is made from live vaccinia virus (it does not contain variola virus) and transmission is possible from the vaccination site up to 3 weeks after vaccination. The shedding period may be less for revaccination. The inoculation site is generally considered infectious from the time just after vaccination until the scab separates from the skin. Vaccinia is transmitted by close contact and can lead to the same adverse events in an infected contact as in the vaccinee. The inoculation sites should remain covered and vaccinees should wash their hands immediately after touching vaccination sites or changing dressings. The smallpox vaccination is generally considered safe, but is contraindicated in patients who have, or are in close contact with, those who have atopic dermatitis (eczema) regardless of the severity, skin diseases that disrupt the epidermis, pregnant women or women who plan on becoming pregnant within 1 month after vaccination, and immunocompromised patients. Others who should not receive the vaccine include those who have an allergy to a component of the vaccine, are breast-feeding, are using ocular steroids, have moderate-to-severe intercurrent illness, or are younger than 18 years of age.

The CDC has an excellent web site for health-care providers who wish to learn more about the smallpox vaccine: www.bt.cdc.gov/training/smallpox-vaccine/reactions/default.htm

### *Nurses: Delay Vaccination Program*

Meanwhile, not everyone is happy with the national smallpox vaccination program. Recently the American Nurses Association (ANA) requested that the Bush administration delay the smallpox vaccination program until certain safety issues can be addressed. Specifically, the ANA is seeking information regarding potential transmission of vaccinia virus to family members of vaccinated nurses, coverage of medical costs related to vaccination, safety of the vaccination materials, adequate educational materials and staffing issues, and job security issues related to the vaccination program. Others such as Thomas Mack, MD, MPH, argue in the Jan. 30 edition of the *New England Journal of Medicine* that

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. Telephone: (404) 262-5517. E-mail: robin.mason@ahcpub.com. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

smallpox is overrated as a bioterrorist weapon. His view is that the current vaccination policy would provide little protection and the cost from vaccine complications would outweigh any benefit (*N Engl J Med*. 2003;348:460-463). However, a special article in the same issue developed scenarios of smallpox attacks and reviewed possible outcomes of control policies. Their analysis favors a program of prior vaccination of health care workers but favors vaccination of the public only in the likelihood of a national attack, or multiple attacks is very high (*N Engl J Med*. 2003;348:416-425).

### Viagra Effective for Depression Treatment

Sildenafil (Viagra) is an effective treatment for antidepressant-associated sexual dysfunction in men. The drug was tested in a multicenter randomized double-blind placebo-controlled trial. Ninety men with major depression in remission on SSRI antidepressants were randomly assigned to take sildenafil (50 to 100 mg) or placebo for 6 weeks. Men who were most affected by antidepressant-associated sexual dysfunction were significantly more likely to improve with sildenafil (24/44, 54.5% response rate) vs placebo (2/45, 4.4% response rate) ($P < .001$). Erectile function, arousal, ejaculation, orgasm, and overall satisfaction measures improved significantly with sildenafil compared with placebo (*JAMA*. 2003;289:56-64). This study is important because sexual dysfunction is a common cause of noncompliance with serotonin reuptake inhibitors, and use of sildenafil may improve compliance with antidepressant treatment.

### Finisteride/Doxazosin no Better than Placebo for Urinary Obstruction

Finisteride (Proscar) is no better than placebo when used in combination with doxazosin for the treatment of urinary obstruction due to benign prostatic hypertrophy, according to the recently published Prospective European Doxazosin and Combination Therapy (PREDICT) trial. These findings come in contradiction to the Medical Therapy of Prostatic Symptoms (MTOPS) trial published in May 2002, which showed a benefit of the combination of finasteride and doxazosin. In the current study, more than 1000 men were randomized to doxazocin, finisteride 5 mg per day, the combination of both, or placebo. The groups receiving doxazocin alone or in combination with finisteride had significant improvements in total maximal urinary flow rates and International Prostate Symptoms Score compared to the finisteride alone group and placebo group ($P < .05$). There was no significant difference between treatment with finisteride and placebo. Doxazosin was initiated at 1 mg per day and titrated to a maximum of 8 mg per day. All treatments were well tolerated (*Urology*. 2003;61:119-126).

Sildenafil, however, may be effective of relieving obstructive urinary symptoms in men who use the drug on a regular basis. British researchers looked at 112 men with erectile dysfunction at 1 and 3 months after taking sildenafil as needed before sexual intercourse. Only 20 of the 112 men complained of lowered urinary tract symptoms, but of those men, improved urinary scores at 3 months strongly correlated with improvement in sexual function. The authors suggest that an increase in nitric oxide associated with the resumption of normal sexual activity may be responsible for the improvement in urinary symptoms (*Br J Urol Int*. 2002;90: 836-839).

### Serevent Receives 'Dear Doctor' Letter

GlaxoSmithKline has issued a "Dear Doctor" letter regarding its asthma bronchodilator salmeterol (Serevent). The warning is based on interim results from a large study of salmeterol that was initiated in 1996. The Salmeterol Multi-center Asthma Research Trial (SMART) was a postmarketing study designed to investigate reports of several asthma deaths associated with use of salmeterol. Analysis of the interim results showed a trend "toward a greater increase in asthma deaths and serious asthma episodes" with the largest increase in African-American patients. Data on almost 26,000 patients were available for analysis. While there was no significant difference for the primary end point of combined respiratory related deaths and respiratory related life-threatening experiences including incubation and mechanical ventilation between salmeterol and placebo, a higher, but not statistically significant number of asthma related life-threatening experiences including deaths occurred in the salmeterol group. The number of adverse events reached statistical significance in African-Americans who represented 17% of the study. No other ethnic group drew any conclusions. The use of inhaled corticosteroids reached only 47% in the entire population of the SMART study. Because of these findings, GlaxoSmithKline has decided to discontinue the study and continue reviewing data from the interim analysis. The FDA is involved in this process and will likely require label changes for Serevent that will reinforce guidance on appropriate and safe prescribing. ■