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DWI vs. Post-mortem Examination of Patients with Acute Stroke: In Search of a Gold Standard

A B S T R A C T & C O M M E N T A R Y

Source: Kelly PJ, et al. Diffusion MRI in ischemic stroke compared to pathologically verified infarction. *Neurology*. 2001;56:914-920.

Diffusion weighted imaging (dwi) has become the new standard in the diagnosis of acute stroke. Because DWI directly detects tissue ischemia, it has a sensitivity and specificity far superior to standard T2 or FLAIR sequences. As previous *Neurology Alert* reviews have noted, however, DWI does not correlate directly with stroke in every case. False-negative "misses" and false-positive "mistakes," do occur. Not every stroke is assured to produce a DWI signal and many other entities other than stroke, such as glioma, demyelination, or seizure, may produce DWI abnormalities. In the current report, Kelly and colleagues compare DWI against the most certain marker of stroke, infarction of brain tissue pathologically verified at autopsy.

Kelly et al report on 11 patients studied retrospectively who underwent DWI scanning for evaluation of stroke syndromes and who subsequently died. Each underwent full autopsy examination, including gross and microscopic analysis. A total of 25 strokes were detected at autopsy; 23 of which were seen on DWI. Two strokes detected by DWI were not found at autopsy. The sensitivity, specificity, positive predictive and negative predictive values for detection of stroke using DWI were, therefore (in a small cohort), 88.5%, 96.6%, 85.2%, and 97.4%, respectively.

Three additional cases were studied prospectively, with the neuropathologist blinded to the DWI findings. The correlation between DWI and pathologically proven strokes was virtually 1:1, including tiny cortical emboli. In 1 case, a large left posterior cerebral artery territory infarct, pathologically aged 12-24 hours, was not detected by DWI and almost certainly occurred during the interval between the last MRI scan and the patient's death. Similarly, Kelly et al describe 2 DWI "misses" in the retrospective cohort, both of which were found in patients with endocarditis who were intubated, sedated, and likely sustained ongoing emboli between the last MRI and

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death. The 2 possible DWI "mistakes" probably did represent tiny strokes missed on 1 cm autopsy slice specimens. Finally, 2 other patients who were initially thought to have presented with stroke based on clinical exam, were ultimately diagnosed with Todd's paralysis and metabolic encephalopathy. In these cases, both DWI and pathological examination confirmed the absence of an ischemic lesion.

COMMENTARY

The data presented by Kelly et al represent an important correlation between radiologic data and neuropathology. DWI is at least 90% accurate, and probably more, in diagnosis of acute stroke. But DWI or any imaging procedure must ultimately be interpreted in the context of the clinical history and neurological examination. The majority of the autopsy specimens in Kelly et al's study were not reviewed blindly. It is, therefore, possible that the pathologist actually used the DWI to assist in localizing areas of infarction at autopsy. Although Kelly argues that, "neuropathologists at our institution do not routinely examine neuroimaging data prior to sectioning the brain," it is likely that pathologists reviewed clinical histories, and ultimately CT, MRI, or other associated data before signing out their final conclusions. Any comparison of DWI to autopsy data is prone to the possibility of interim events occurring between the most recent DWI and the time of death or the chance of the pathological prosector missing one or more tiny infarcts. Unless DWI is performed immediately postmortem or neuropathological methods are 100% diagnostic of neuronal ischemia, the MRI will remain just one element in a comprehensive exercise of clinicopathological correlation. **—alan z. segal**

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CADASIL: An Autosomal Dominant Genetic Stroke Disorder

ABSTRACT & COMMENTARY

Source: Bousser MG, Tournier-Lasserve EJ. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy: From stroke to vessel wall physiology. *J Neurol Neurosurg Psychiatry.* 2001;70:285-287.

In 1976, bousser identified a large french family that contained several members who suffered small strokes related to abnormalities of small cerebral arteries at a relatively low age. She identified 8 other families reported in the literature between 1955-1992 and defined their mutual specific qualities as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). In 1993, the gene was identified on chromosome 19 q12 and was specifically identified as Notch 3 in 1995. A molecular diagnostic test is now available for diagnosis. Subsequently, sporadic cases were identified, although the hereditary genes continue to be the cause.

CADASIL produces various symptoms and signs between individual patients, but the principal disturbances consist of ischemic subcortical strokes, dementia, migraine with aura, and emotional-intellectual disturbances. Migraine with aura, if at all, usually appears during the late 20s or early 30 years. Randomly occurring ischemic strokes or apathetic behavior usually strike patients aged 40-50 years. The following 15 years usually represent an ultimate tragedy of severe, mute dementia. Most CADASIL patients die by age 65, although a few "odd ball" persons can remain asymptomatic in their eighth decade.

Diagnosis by the above clinical criteria can be relatively straightforward, particularly when small strokes follow late delayed migraine. MRI consistently identifies hypersignals of T2-weighted images in the periventricular and centrum semiovale. Additional lesions con-

sistently affect the basal ganglia (denying multiple sclerosis) and the pontine tegmentum. Eventually, multifocal, deep leucoencephalopathic infarcts that spare the cerebral cortex appear. Specific diagnosis can be made by skin-muscle biopsies which demonstrate thickening of smooth arteriopathic muscle cells that eventually degenerate. If possibly available, electron microscopy can diagnose the disease by identifying granular, osmophilic materials in smooth arterial muscle.

COMMENTARY

In the last 15 years, Bousser has clinically and genetically identified a new form of inborn vascular disease that selectively, severely damages the brain. Apparently, however, absolute diagnosis can be made by skin-muscle biopsy and the finding of the Notch 3 mutation of chromosome 19. Absolute diagnosis (of CADASIL) also can be suggested by MRI T2 scanning plus pathological diagnoses of skin-muscle biopsy. As she states, "Next important steps will be to determine whether mutations lead to inhibition or activation of the Notch 3 signaling pathway and whether Notch 3 accumulation occurs in a ligand dependent or independent context." **—fred plum**

Botox Ameliorates Problems in Swallowing Disorders

ABSTRACT & COMMENTARY

Source: Porta M, et al. Treatment of sialorrhea with ultrasound guided botulinum toxin type A injection in patients with neurological disorders. *J Neurol Neurosurg Psychiatry.* 2001;70:538-540.

Injection of botulinum toxin has revolutionized the treatment of focal dystonia. Approved by the FDA in 1990, botulinum toxin injection is now the treatment of choice for patients with blepharospasm, torticollis, oromandibular dystonia, spasmodic dysphonia, and hemifacial spasm. The dramatic response to treatment and the safety of the procedure led investigators to apply this technique to a variety of other conditions, including bruxism, lower esophageal and rectal spasms, spasticity, tics, and hyperhidrosis.

Botulinum toxin exerts its effect by inhibiting the release of acetylcholine at the neuromuscular junction. In the last 2 years, several studies have shown that injection of toxin into the parotid gland is an effective treatment for patients with excess saliva. Excessive drooling or salivation usually accompanies neurologic conditions in which coordination of swallowing is impaired, including ALS, head trauma, cerebral palsy, and Parkinson's disease. Among Parkinson patients followed at the Neurological Institute of New York, sialorrhea is a common complaint. In 5% of these patients, uncontrolled salivation becomes a major source of hygienic and psychosocial embarrassment. We have found that medical treatments for sialorrhea (typically anticholinergic drugs) are usually ineffective and poorly tolerated by older patients.

In this paper, Porta and colleagues describe their experience injecting botulinum toxin into the parotid and submandibular glands of patients with excessive sialorrhea. Ten patients were enrolled in this open-label study, 4 with ALS, 2 with Parkinson's disease, and 1 each with primary sialorrhea, SSPE, cerebral palsy, and head trauma. Fifteen to 40 units of Botox (botulinum toxin type A) were injected into each parotid gland, and 10-15 units were injected into each submandibular gland. Porta et al defined the anatomy of the parotid and submandibular glands and the trajectory of the facial nerve using ultrasound. Patients rated their improvement using a visual analogue scale. Sialorrhea lessened within 5 days of injection which improved patients an average of 61%, and maintained the benefit an average of 4.7 months. There were no adverse events and side effects were minimal.

COMMENTARY

This is a convincing study, showing that Botox is an effective treatment for patients with troubling sialorrhea. Ultrasound guidance is a useful tool to ensure optimal injection of the parotid gland, and it is probably required to inject the submandibular gland, which normally provides up to 70% of daily saliva production. The degree of improvement in sialorrhea is comparable to other studies, and the technique is well tolerated and safe. Fortunately, although the benefit remained only a bit longer than 4 months after injection, repeated injections appeared to sustain the improvement.

Unfortunately, a major limitation to this technique is the cost of the treatment. Botulinum toxin is extremely expensive, between $4 and $5 per unit, or $400 to $500 for an average sialorrhea injection. This does not include the injection fee. At present, Medicare and most managed care plans do not cover this procedure, and it is unclear whether or not physicians will be reimbursed if they perform it. This is unfortunate, as the technique effectively treats an often troubling symptom for which alternative treatments are not adequate. **—steven frucht**

Low-Grade Glioma May Do Better Without Surgical Therapy

ABSTRACT & COMMENTARY

Source: Reijneveld JC, et al. Cognitive status and quality of life in patients with suspected versus proven low-grade gliomas. *Neurology.* 2001;56:618-623.

Management of patients who develop first seizures later than 16-18 years of age usually includes brain imaging which, in the United States, is performed by MRI. Current quality of this technology can identify the probability of low-grade glioma, particularly in first-diagnosed persons younger than 40-45 years. At least in Europe, many neurologists defer early surgical resection or biopsy as well as unproved radiation therapy in these younger persons. Shafqat and colleagues found that low-grade astrocytomas diagnosed in patients between 10-45 years averaged 44 ± 17 months to transform into malignancy (see Plum F. *Neurology Alert* 1999;17:70-71). Survival averaged 58 months. Persons who suffered the onset of similar tumors at age 45 and older averaged only 7.5 months for malignant transformation and died an average of 14 months later for identification.

Reijneveld and associates selected 48 persons with low-grade gliomas who were first diagnosed in 2 groups: 24 were diagnosed at an average age of 38.4 ± 7.6 years based on clinical and brain image findings alone; the other 24 were diagnosed by surgical resection or stereotaxic biopsy at an average age of 32.7 ± years. All patients were studied between June 1998 and July 1999. All were 18 years of age or older and showed nonenhancing supratentorial lesions on MRI or CT. None had signs of progression during at least the 6 months before examination. The nonsurgical group was evaluated 4.4 years after the initial noninvasive diagnosis compared to a 5.5 year lapse for the histologically proved group.

Quality of life represented the given outcome expression between the 2 groups, one presumptive of glioma and the other with a proved diagnosis. Overall, quality of life in either group was less than what 24 healthy controls achieved. The surgical group, however, proved to do worse than the nonsurgical group in quality behavior of life. The surgical group had more complaints, but had insignificantly self-rating cognitive capacities.

Reijneveld et al conclude that young, 18-40-year-old patients with low-grade gliomas inevitably undergo impaired cognitive functioning and they measurably do better in daily behavior than do patients with similar diagnoses who receive early therapy, either surgical removal or radiation therapy.

COMMENTARY

This report is relatively short but states its findings accurately and clearly. Apparently, some of their patients must have been older than 50, thus being vulnerable for a shortened life. That would not be apparent in this report, but Shafqat et al discuss that directly in their report (Shafqat S, et al. *Neurology* 1999;52:867-869). **—fred plum**

Glatiramer Acetate Effects on MRI and Disease Activity in MS

ABSTRACTS & COMMENTARY

Sources: Comi G, et al. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging-measured disease activity and burden in patients with relapsing multiple sclerosis. *Ann Neurol.* 2001;49:290-297; Filippi M, et al. Glatiramer acetate reduces the proportion of new multiple sclerosis lesions evolving into "black holes." *J Neurol.* 2001;248(suppl 2):112; Rovaris M, et al. Effect of glatiramer acetate on brain volume in patients with relapsing-remitting multiple sclerosis. *J Neurol.* 2001;248(suppl 2):27.

In this controlled multicenter study, 239 patients with relapsing MS (including patients with 1 or more relapses in the past 2 years, and 1 enhancing lesion on screening MRI) were randomized to either a glatiramer acetate (GA) treated group, or a placebo group. Patients underwent monthly MRIs and clinical assessments over 9 months. Treatment with GA caused a significant reduction in the total number of enhancing lesions compared with placebo (-10.8, $P = .003$), approximately a 29% reduction, as well as a number of new enhancing lesions ($P < .003$), monthly change in volume of enhancing lesions ($P = .01$), change in volume ($P = .006$), and a number of new lesions seen on T2-weighted images ($P < .003$). There was a decrease in relapse rate of 33% in GA-treated patients ($P = .012$), with 0.51 relapses/subject, vs. 0.76 relapses/subject in the control group. Steroid treatments were required in 33.6% of GA patients vs. 39.2% of patients in the place-

bo arm. All effects increased slowly over time, with significant separation from the control group after 6 months. As expected for the short study period, there were no significant differences in the disability scores between the 2 groups.

Additional MRI data from the same clinical trial presented last month at the European Neurological Society Meeting in Paris showed that while GA appeared to reduce the number of "black holes" being formed on T1 brain MRI, it did not seem to reduce the process of brain atrophy compared to placebo controls in the 9-month study period.

COMMENTARY

Several large clinical trials have been published on the treatment of relapsing forms of MS with different preparations of interferon-beta, documenting consistent benefits for attack frequency, and highly significant reductions in disease activity on brain MRI that could occur within 3 months of drug treatment. It is helpful to have this large series of patients in this controlled clinical trial of GA by Comi and colleagues for comparison. In the study design, changes in disease activity on brain MRI were primary and secondary outcome measures, while relapse rate and other clinical measures were actually tertiary. The study was appropriately powered to demonstrate a benefit within a 9-month period, although effects of a longer treatment period would have been of interest given the long-term nature of such drug therapies. As discussed by Comi et al, the relatively delayed MRI effects of GA may reflect the mechanism of action, whereby induction of regulatory T cells are required to migrate to sites of inflammation in the brain. Interferon-beta, in contrast, may more directly inhibit proliferation and migration of lymphocytes into the central nervous system. Nonetheless, this current study reinforces the MRI and clinical benefits of GA in relapsing MS that had previously been presented in smaller numbers of patients. **—brian r. apatoff**

The Canadian CT Head Rule

ABSTRACT & COMMENTARY

Source: Stiell IG, et al. The Canadian CT head rule for patients with minor head injury. *Lancet.* 2001;357:1391-1396.

The canadian ct head injury group made up of Emergency Medicine leaders has focused on the usefulness of computed tomography (CT) in identifying potentially severe, trauma-induced intracranial hematomas that require neurosurgical intervention. They cite that emergency departments in the United States perform an estimated 270,000 annual CTs in head injuries with a total cost of $135-216 million dollars. Canada has varying records of using CT for acute head trauma in large different hospitals but their present numbers considerably vary among the different institutions.

Ten Canadian community and teaching institutions enrolled consecutive adult patients who arrived at their emergency departments after sustaining minor head injury. Accepted patients had received blunt head trauma, brief losses of consciousness (LOC), definite amnesia or disorientation, but all amounting to 13-15 Glasgow Coma Scale (GCS) ratings at onset, (15 GCS ratings = no severe abnormalities, but patients with < 13 GCS at any time always had CT scans). The time window for waiting to reach the hospital and enter the evaluations lasted for 24 hours following the trauma.

A total of 2078 high-risk patients fulfilled the above criteria for GCS score and received immediate CT scans associated with the injuries in the CT Head Rule. Stiell and colleagues define the CT Head Rule as follows: high-risk factors (for neurological intervention) include: GCS score < 15 at 2 hours after injury; suspected open or depressed skull fracture; any sign of basal skull fracture (hemotympanum "racoon" eyes, cerebrospinal fluid otorrhea/rhinorrhea, Battle's sign); vomiting ≥ 2 episodes; age ≥ 65 years. Medium risk factors (for brain injury on CT) include: amnesia before impact > 30 min; and dangerous mechanism (pedestrian struck by motor vehicle, occupant ejected from motor vehicle, fall from height > 3 feet or 5 stairs). They defined minor head injury as witnessed loss of consciousness, definite amnesia, or witnessed disorientation in patients with a GCS score of 13-15.

Stiell et al indicate that any 1 of the above 5 high-risk factors have the potential for requiring neurosurgical intervention, a fact indicator that CT is imperative. Most American hospitals presently would also perform the medium risk CT, but minor risks rarely need a CT for management.

COMMENTARY

This report provides statistically strong indications for obtaining CT scans as quickly as possible for trauma patients who suffer a high symptomatic risk of progressive injury or death unless surgical treatment is supplied. As is true in the United States, medium-risk patients who arrive at small hospitals having no CT scanners should be sent promptly to more comprehensive institutions with a strong trauma service that is active a full 24 hours a day! Most such patients who need CTs within 24

hours post-trauma should be in the hands of alert doctors to act if worsening appears. **—fred plum**

Post Mild Traumatic Brain Injury Shows Dissociations Between MRI and SPECT

ABSTRACT & COMMENTARY

Source: Hofman PA, et al. MR imaging, single-photon emission CT, and neurocognitive performance after mild traumatic brain injury. *AJNR Am J Neuroradiol.* 2001;22:441-449.

This report describes the presence of moderately severe, abnormal neurological symptoms and their outcomes in 21 persons following mild traumatic brain injury. The literature indicates that symptoms of headache, dizziness, impaired memory, and difficulty in concentration follows 80% of even mild, unexpected head injury. About three-fourths of such reactions disappear within a week or so. This report describes the post-traumatic findings of 21 consecutive, previously healthy persons younger than 50 years of age. Each subject suffered less than 20 minutes of post-traumatic loss of consciousness and/or of amnesia for less than 6 hours. MR images, SPECT quantification, and neurocognitive testing were applied to every subject. "Cognitive tests" included Visual Verbal Learning, Stroop Color Word, Concept Shifting, Letter Digit Substitution, Fluency, and Motor Choice Reaction tests.

Mean age of the 21 subjects amounted to 22.8 years. Mean post-traumatic unconsciousness averaged 4 minutes and the amnesic period lasted 67 minutes. All 21 patients had MRI examinations and 18 had HMPAO-SPECT testing.

Twelve patients had abnormal MRI findings and abnormal SPECT findings. Only 7 patients displayed both abnormalities. As Hofman and associates put it, "the agreement between MR and SPECT studies was . . . poor." FLAIR MR images brought out a larger number and size of abnormalities (mean = 3.61) than did the T2-weighted MR images. Extracerebral hemorrhages affected 2 persons, but 12 suffered a total of 42 lesions in the frontal lobe and/or 16 lesions in the temporal lobe. Neither age, education, nor trauma severity was selectively associated with the MR findings. Brain atrophy appeared at 6 months in the patients who had abnormal post-traumatic MRs.

Neurocognitive evaluations demonstrated a modest abnormality (0-21) 2 months after the accidents but this disappeared (0.45) after 6 months.

Post-traumatic complaints rated on a 28-item questionnaire at 2 months (normal MR = 13.33, abnormal 8.11), changed only slightly at 6 months (12.57 normal MR, abnormal MR 7.30). Long-term complaints included forgetfulness, difficulty in concentration, trouble with word finding, and mental slowness. There was no consistent association between neurocognitive results and SPECT findings. Most of the abnormal SPECT findings indicated regions of hypoperfustion. Explanation of this particular association is presently no more than guess work.

COMMENTARY

As Hofman et al put it, "the most important finding in our series of brain trauma patients was the high prevalence of brain lesions." This may be true, but was there any selection of patients who especially appeared to have surface body injury? Granted that it might be useful to apply brain imaging to all patients who have more than 90 minutes of post-traumatic amnesia, but, with the exception of extra dural hematomas, how does that step improve patient care? Shouldn't CT scanning provide a much less expensive but equally effective identification for such hematomas?

As for the neuropsychological variations in this cohort of post-traumatic patients, they seem to be dissociated from the severity of the tissue abnormalities. Given the fact that all of the formal psychological deficits disappeared within 6 months, it appears merely that their source reflected temporary psychological disruption rather than tissue damage.

Until some therapy can be found to repair brain structure, your editor doubts the value of applying expensive MRI or SPECT tests for post-traumatic head injury of mild-to-moderate degree. If a research plan on the topic can be funded, follow-up material should last at least 5 years. Otherwise, these data only risk legal invitation for relatively modest injuries. **—fred plum**

More on Spontaneous Intracranial Hypotension

ABSTRACT & COMMENTARY

Source: Schievink WI, et al. Spontaneous intracranial hypotension mimicking aneurysmal subarachnoid hemorrhage. *Neurosurgery.* 2001;48:513-517.

The clinical features, pathogenesis, and treatment of spontaneous intracranial hypotension (SIH)

were recently reviewed in *Neurology Alert* (Caronna JJ. *Neurology Alert* 2001;19:43-44.) Nevertheless, the present study is notable because it describes an unexpected mode of presentation of that condition. Among 28 patients with a documented cerebral spinal fluid (CSF) leak, 4 presented with an excruciating headache of instantaneous onset ("thunderclap headache") as the initial manifestation of SIH. The mean age of the 4 patients (2 women and 2 men) was 35 years (range, 24-45). A stiff neck was present in 3 patients who were diagnosed initially as having a subarachnoid hemorrhage (SAH) and, therefore, they underwent emergency brain CT scanning, lumbar puncture, and cerebral angiography, all of which were normal. All 4 patients had meningeal enhancement and brain sagging on MRI scanning. Treatment consisted of ligation of 2 meningeal diverticula in 1 patient and repair of a dural tear caused by an osteophyte in another. Two patients who did not have a structural lesion identified on CT myelography underwent successful epidural blood patching.

COMMENTARY

Schievink and colleagues found that thunderclap headache was a relatively common (4/28 patients) presentation of SIH, an observation that has not been reported previously (Day JW, Raskin NH. *Lancet.* 1986;2:1247-1248). Therefore, they have added another diagnosis to the differential diagnosis of thunderclap headache that already includes SAH, cervical artery dissection, cerebral vein thrombosis, pituitary apoplexy, and migraine.

The diagnosis of acute severe headache involves the exclusion of serious intracranial disease, therefore, the initial evaluation of thunderclap headache must include a CT scan and lumbar puncture to rule out bleeding and increased intracranial pressure. If the findings on these tests are normal, then Schievink et al suggest the best subsequent investigation is a contrast-enhanced brain MRI rather than cerebral angiography. **—john j. caronna**

Brief Alerts

Botulism: Making the (Electro)Diagnosis

Source: Gutmann L, Bodensteiner J. Electrodiagnosis of botulism—revisited. *J Clin Neuromusc Dis.* 2001;2:121-122.

Botulism may be correctly diagnosed at the bedside in a timely fashion using electrodiagnostic criteria, provided that mindfulness to detail avoids pitfalls. Compound muscle action potential (CMAP) amplitudes should be low but are generally not so in every nerve. Consequently, several nerves must be studied. Decrement of the CMAP amplitude on repetitive low-frequency (2 Hz) nerve stimulation is inconsistent and unreliable for botulism but should be pursued. Botulism may, after all, not be the correct diagnosis! CMAP increment on rapid (tetanic) repetitive high-frequency (20-50 Hz) nerve stimulation for 10 seconds is the electrical sine qua non for diagnosis, but again must be sought in several nerves if initially elusive. It is painful but unavoidable in infants. In adults, recording CMAP amplitude pre and post 10 seconds of maximal contraction can supplant tetanic stimulation. Increments less than 20% are physiologic and of no clinical significance. Increments of 23% to 313% may be seen in 92% of cases. Perhaps of greatest value is observing CMAP changes in the later post-tetanic (or post-exercise) period. Post-tetanic facilitation (increment) persists for several minutes in botulism, whereas it lasts less than a minute in other junctionopathies, where post exercise exhaustion may be seen. This is absent in botulism. **—michael rubin**

Steroids for Sudden Hearing Loss

Source: Alexiou C, et al. Sudden sensorineural hearing loss: Does application of glucocorticoids make sense? *Arch Otolaryngol Head Neck Surg.* 2001;127:253-258.

Sudden sensorineural hearing loss (ssnhl), though infrequently seen by neurologists, is a common disorder, with an incidence of 1 in 3000. Suspected etiologies include viral infection, microvascular occlusion, and autoimmune disorders. Treatment guidelines do not exist although rheotherapy, antiviral agents, nonsteroidal anti-inflammatory drugs, and corticosteroids are often administered.

Retrospective analysis of audiograms of 603 SSNHL patients was undertaken to assess the efficacy of glucocorticoids for SSNHL. Patients had received intravenous (IV) pentoxifylline (a blood flow-promoting agent, Trental, 100 mg) without (n = 301) or with (n = 302) IV prednisolone (500 to 1000 mg for 3 days). IV prednisolone was followed by oral prednisone (100 mg taper over 16 days) if the former did not produce improvement.

Glucocorticoid-treated patients with low and middle frequency SSNHL demonstrated significantly bet-

ter recovery of hearing compared to the nonsteroid treated group. Similarly, SSNHL patients at all frequencies demonstrated significantly better recovery with glucocorticoids plus pentoxifylline, compared to the pentoxifylline-only treated group. The recommendation is clear: glucocorticoids are advocated for patients with SSNHL. Add pentoxifylline for good measure. **—michael rubin**

CME Questions

26. CADASIL can be specifically diagnosed best by which test?
a. Clinical small strokes after 45 years of age
b. A diagnostic MRI with T2 signals
c. A molecular diagnostic test
d. Normal histology of a skin muscle biopsy

27. Which of the following conditions may present with thunderclap headache?
a. Pituitary apoplexy
b. Ruptured cerebral aneurysm
c. Cerebral venous sinus thrombosis
d. Spontaneous CSF leak with intracranial hypotension-hypovolemia
e. All of the above

28. In a patient with thunderclap headache and a negative CT and LP, the next best test to perform is:
a. MRI of the brain without contrast.
b. cerebral angiography.
c. MRI of the spine or CT myelogram.
d. MRI of the brain with contrast.
e. None of the above

29. The most specific electrodiagnostic abnormality seen in botulism is when:
a. decrement of the compound muscle action potential amplitude on repetitive low-frequency (2 Hz) nerve stimulation.
b. compound muscle action potential increment on rapid (tetanic) repetitive high-frequency (20-50 Hz) nerve stimulation for 10 seconds.
c. post-tetanic facilitation (increment) persists for several minutes in botulism.
d. compound muscle action potential amplitudes are low.
e. there are no specific electrodiagnostic abnormalities in botulism.

30. Botox injections:
a. are an effective treatment for patients with sialorrhea.
b. are extremely expensive.
c. in the Porta et al study caused no adverse events, and side effects were minimal.
d. All of the above

In Future Issues:

Neurodegenerative Diseases and Prions