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Can Human Fetal Striatal Neuroblasts Halt or Only Briefly Improve Huntington's Disease?

ABSTRACTS & COMMENTARY

Sources: Bachoud-Lévi AC, et al. *Lancet* 2000;356:1975-1979; Freeman BF, et al. *Proc Natl Acad Sci U S A* 2000;97:13877-13882.

Can human fetal striatal neuroblasts halt or only briefly improve Huntington's disease (HD)? The answer to this question appears to be yes for the first few years, but length of time and/or complications have not yet been thoroughly tested.

Bachoud-Levi and colleagues at INSERM in France describe an open-label pilot study consisting of injecting normal human fetal striatal neuroblasts into the striatum of clinically impaired patients with HD.

Animal testing has been successful in such injections, and no inflammatory reactions after the implanting of functionally normal striatal neuroblasts have been identified. Indeed, their immediate effects ameliorated excitotoxins or metabolic toxins at the point where the injected cells were placed in the striatum. Following these favorable reactions in animals, Bachoud-Levi et al selected 10 relatively healthy controls with HD to serve as a clinical baseline. At the same time, they also selected and treated by striatal neuroblasts five HD patients who were moderately impaired from the disease. The first injected tissue was taken from normal human fetuses 7.5-9 weeks old and was transferred in small blocks into the right HD striatum. Twelve months after the first successful injections, fetal striatal neuroblasts were inserted into the left striatum. Immunosuppressive therapy was applied from the start until 12 months after the second injection. Because of Bachoud-Levi et al's firm intention for accuracy, they spent one and a half years evaluating baseline behavioral assessments using psychological and neurophysiological test intervals before the first injections. As a result, they were continued up until 24 months after the first implantation. Both electrophysiological and PET plus MRI were used as diagnostic tools. Twenty-two untreated, similarly affected HD patients were also followed by similar neuropsychological and psychological tests. Most of these (with 1 exception) doubled their neuropsy-

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chological defects and their mean chorea intensity.

The five patients who were grafted had suffered baseline HD symptoms for 2-7 years prior to the graft. After the graft, three of the five showed either an increase or stable striatal metabolism 24 months following the first injection. Their functional improvements included cycling, various rigorous home tasks, and odd jobs. One resumed working. Family members considered that both thinking and physical efforts improved in the treated HD patients. Patients 1 and 2 recovered evoked bilateral N_20 waves but another patient lost one. The other two patients resumed their previously steady deterioration and showed a greater metabolic decay in both the images of their striata and their worsening clinical behavior. Unfortunately, Bachoud-Levi et al state that the three "improved" HD patients began to slow down motor function as the three years approached their limit. On the whole, however, attention and executive capacity remained and their total improved scores have now lasted for three years. One of the three patients improved after the first one-sided implant, but started to regress slowly five months after the second when a cyst appeared in the left, second-injected putamen. As a pilot study, Bachoud-Levi et al concluded that all together, these somewhat encouraging results may lead to a large-scale multicentered study in a measurably larger cohort.

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Freeman and colleagues from The University of South Florida, as well as several other academic institutions, similarly injected normal fetal striatal tissue into the degenerating striatum of seven patients with HD. One of these patients, a 54-year-old man, had received a total of 10 such cell implants into both sides of his striatum 18 months before he suddenly died from chronic heart disease. Autopsy disclosed three transplants in the right putamen and two in the left putamen. The implants were calculated as providing 9.8% of the total remaining left putamen and 7.6% on the right. All grafts were interpreted as being functional by neuronal markers, namely the normal huntingtin protein that possesses less than 35-37 CAG repeats. Normal cell protein-associated immunostained cells appeared in both graft tissues, with minimal abnormal huntingtin identified in the transplants. The findings indicate that human fetal tissue, which arises from striatal primordia, can withstand functional transplantation into an abnormal putamen for at least 18 months. Inflammation was not found in the post-mortem samples and a number of natural markers that imply functional pre-mortem activity were identified.

In addition, both Bachoud-Levi et al and Freeman et al reported additional clinical effects of fetal transplants into patients with HD. These both appear in abstract form in the AAN Program book for 2000 on page A 153 and theie contents are referred to in the next paragraph.

Guara and colleagues report PET/MRI values in the five patients described previously by Bachoud-Levi et al. Patient 1 was clinically improved and CMR glu increased in both striata one year after fetal neuroblasts implantation. Patients 2 and 3 showed right striatal CMR glu increases from + 0 to 22% one year after the right graft but only -11 to 4% on the left. Patient 4 at first improved but then declined and patient 5 had no benefit from the graft.

Hauser and colleagues report on pilot evaluation of human fetal striatal transplantation in HD. They indicated that they transplanted seven patients with staged fetal striatal grafts ranging from 2-8 implants per side. All patients received cyclosporine for two weeks before and six months after the surgery. Five patients had undergone at least nine months after transplantation. Two of the nine developed subdural hematomas (SDH) following implantation and necessitated drainage. Despite evacuation, one of the two failed to return to cognitive baseline. One patient's condition worsened from bilateral SDH, but four patients who reached one year after implantations had improved their Unified Huntington's Disease Rating Scale means from 34.5 to 27.8. The lower basemark reflects improvement.

COMMENTARY

These four reports from two high-quality neurological centers provide great hope for future striatal gene generation in HD. However, Bachoud-Levi et al only had a three-year follow-up and Freeman et al reported a small average of improvement over more than a year. Hints of developing larger groups of patients with human fetal transplants and still-delicate neurosurgical proceedings have been suggested. As things go presently, evidence to date indicates that sustained improvement may decline after three postsurgical years. Strong improvement has not occurred much longer than two years after the present initial implantation. Hopefully, the experimenters will become able to improve longer than three years in length with an incidence rate of successful transgenesis of at least 80%. **—fred plum**

Spontaneous CSF Hypovolemia: A Syndrome Characterized

ABSTRACT & COMMENTARY

Source: Chung SJ, et al. *Neurology* 2000;55:1321-1327.

Previous studies have described the syndrome of spontaneous intracranial hypotension as including: orthostatic headache, low cerebral spinal fluid (CSF) pressure, and diffuse pachymeningeal gadolinium enhancement on MRI without antecedent trauma or lumbar puncture (Fishman RA, et al. *Neurology* 1993; 43:609-611; Pannullo SC, et al. *Neurology* 1993;43:919-926). The underlying pathogenic mechanism is thought to be a spontaneous CSF leak from a spinal meningeal diverticulum or a dural tear (Schievik WI, et al. *J Neurosurg* 1996;84:598-605). Atypical patents, however, have been reported including those without headache or with nonpositional headache; without pachymeningeal enhancement on MRI; and with clinical signs of encephalopathy, cervical myelopathy, or parkinsonism (see article for references). In addition, the identification of patients with typical symptoms and MRI images but without CSF hypotension has caused the term "CSF hypovolemia" to become the preferred name for this syndrome.

Chung and associates retrospectively studied 30 consecutive patients with the syndrome of CSF hypovolemia admitted to the Asian Medical Center in Seoul, Korea, between 1995 and 2000.

Patients were included who met at least two of the following three criteria: orthostatic headache, low CSF pressure, and diffuse pachymeningeal enhancement on cranial MRI. Two patients did not undergo CSF examination and one patient had a normal CSF opening pressure despite the presence of multiple CSF leaks on radioisotope cisternography.

There were 10 men and 20 women aged 25-53 years (mean 37 ± 8.4). No patients gave a history of head or neck trauma. Seven patients had possible causes of CSF leakage including, in one patient each, chiropractic manipulation, playing golf, swimming, and yoga exercise. Two patients each reported prior vigorous physical activity and severe coughing.

All patients had orthostatic headaches that were variously described as tugging in 10, pulsating in four, pressing in three, and splitting in two. The locations of the headaches are shown in Table 1. The location of the symptoms in addition to headache are shown in Table 2. One woman with bilateral subdural hematomas also had disorientation, memory loss, decreased verbal output, and bradykinesia.

Table 1
Location of Orthostatic Headaches

Site	Number of patients
Whole head	15
Occipital	7
Bifrontal	3
Occipital and bifrontal	3
Bitemporal	2
Posterior neck pain	12

CSF findings were clear in 19, xanthochronic in three, and traumatic in four. Thirteen patients had a CSF pleocytosis, usually up to 50 cells and mostly lymphocytes. Twenty patients had an increased level of CSF protein, the highest being 566 mg/dL. CSF glucose concentration was normal in all patients.

Brain MRI showed diffuse pachymeningeal gadolinium enhancement in 10 of 23 patients. Subdural fluid collections with mass effect were detected in four patients. There was MRI evidence of brain descent in 11 patients. Radioisotope cisternography was abnormal in 21 of 23 patients and showed CSF leaks in 12 *(see Table 3)*.

Overall, headache resolved in all but one patient. Seven patients were treated with bed rest, analgesics, and hydration; 23 with epidural blood patches, and two

Table 2

Orthostatic Symptoms in Addition to Headache

Symptom	Number of patients
Nausea	16
Dizziness	9
Plugged ear(s)	6
Tinnitus	6
Neck stiffness	5
Cervic radiculopathy	2
Blurred vision	1
Diminished hearing	1

of them also had surgical drainage of subdural hematomas. In 18 patients headaches resolved completely, and in 11 only partially. The rate of complete resolution of headache (70%) was greater in those who received epidural blood patches as compared with those who received only supportive treatment (29%). In those who received blood patches, complete resolution of headache was achieved less often in the five patients with multiple CSF leaks than in those with a single leak.

COMMENTARY

This study of a large number of patients with spontaneous CSF hypovolemia syndrome provides useful information, although patients' symptoms were similar to those in other published series. The results indicate that epidural blood patch is an effective treatment in most patients except those with multiple sites of CSF leakage in whom it was less often successful.

As *Neurology Alert* went to press, the following relevant tidbit about CSF hypovolemia caught our eyes from Alvarez-Linera and colleagues (*Neurology* 2000; 55:1895-1897). They briefly report that all 11 female patients with the hypotension syndrome possessed an enlarged pituitary gland (similar findings have been noted by Shimazu and colleagues in a Japanese journal and an abstract by Mokri and Atkinson in *Ann Neurol* 1999;46:475). Alvarez-Linera et al, however, found that the pituitary swelling disappeared in all of their patients when they recovered from the hypotension syndrome. They attribute the temporary transient anatomic change of the pituitary gland to edema caused by the intracranial venous sinuses engorged by increased venous pressure. To your editor's knowledge, studies of pituitary function have not yet been undertaken. **—john j. caronna**

Table 3

Location of CSF Leaks Determined by Radioisotope Cisternography

Site of leak	Number of patients
Cervicothoracic junction	3
Thoracic	2
Thoracic-lumbar junction	2
Lumbar	5
Multiple	5
Cisterna magna (faint)	2

Can Warfarin be Stopped Safely in Patients at High Risk for Stroke?

ABSTRACTS & COMMENTARY

Source: Phan TG, et al. *Arch Neurol* 2000;57:1710-1713; Hacke WS. *Arch Neurol* 2000;57:1682-1684.

Stopping warfarin therapy in patients with prosthetic cardiac valves or atrial fibrillation (AF) may be a source of concern for both physicians and patients who fear that a stroke may occur during this vulnerable time period. These risks are quite exaggerated. Given the overall risk of stroke on a yearly basis in these conditions (4% in patients with a prosthetic valve and approximately 12% in patients with AF), the risk of a short interruption of warfarin is probably minute. The report by Phan and associates from the Mayo Clinic confirms this. As these data suggest, the stroke risk among patients taken off warfarin for about 7-14 days was only 3-5%.

This report retrospectively reviews the records of 141 patients suffering an intracerebral hemorrhage while on warfarin therapy presenting over the past 25 years. Cases were divided into: group 1—patients with prosthetic heart valves (n = 52), group 2—patients with atrial fibrillation and a history of embolic stroke (n = 53), and group 3—patients with a history of recurrent stroke or TIA despite anti-platelet therapy (n = 36). All except nine prosthetic valve patients had mechanical devices. Hemorrhages included: intracerebral hematomas (n = 87), subdural hematoma (n = 43), or subarachnoid hemorrhage (n = 8). Warfarin was withheld from patients for a mean of 10 days, with fresh frozen plasma and vitamin K administered in the acute stages. Three patients suffered ischemic events over 30 days (an occipital embolism in a patient with AF, a lacunar infarct in a patient with a Bjork Shiley aortic valve, and a vertebrobasilar TIA in a patient with a known severe basilar

artery stenosis). The risk of stroke in groups 1, 2, and 3 were therefore 2.9%, 2.6%, and 4.8%, respectively. No patient suffered recurrence of ICH with resumption of anticoagulation. Thirty-day mortality rates from the initial hemorrhage were high: 38% in groups 1 and 2 and 50% in group 3. The majority of this mortality took place in the first 14 days.

In an accompanying editorial, Hacke reviews the data from Phan et al. As he observes and as Phan et al acknowledge, the lengthy period during which cases were collected may have introduced bias due to changing clinical practices. In particular, the high mortality rates may reflect less aggressive surgical intervention strategies and a significant proportion of DNR orders. As Hacke comments, recurrent event rates may be underestimated because patients died within the first two weeks or were managed with a primary focus on comfort measures. Also, follow-up imaging is scant. Recurrent bleeding or new embolic events that were not obviously clinical may have been missed.

Hacke's editorial also draws attention to complementary data from his own institution in Heidelberg, Germany (Bertram M, et al. *J Neurol* 2000;247:209-214). Among 15 Heidelberg patients studied over three weeks, three patients had recurrent bleeding and three suffered embolic events. Both of these rates, in the 20% range, were significantly higher than in Phan et al's data. Recurrent bleeding was restricted to patients with only partially corrected prothrombin times and emboli occurred only in patients who were fully reversed and not treated with intravenous heparin.

COMMENTARY

The need to stop warfarin in the setting of ICH may provide helpful insights into the safety of stopping anticoagulation for short periods of time in other circumstances. In situations much less protean than ICH, it is common clinical practice to briefly withhold warfarin, for instance, before elective surgery or even potentially bloody dental procedures. In rare cases, patients at high risk may be admitted to the hospital to be "covered" with intravenous, unfractionated heparin or treated with subcutaneous low molecular weight heparin injections, but such practices are labor intensive and expensive. If the risk of an intercedent stroke is as low as Phan et al's data indicate, such practices are probably not justified. As Hacke observes, however, Phan et al's data may be an underestimation. The true risk, as suggested by the small Heidelberg series, may be many magnitudes higher. Clearly, anticoagulation should be interrupted for as short a period of time as is possible. Frequent monitoring of prothrombin times as warfarin is withdrawn and paying close attention to its resumption when considered safe afford the best protection against rare, but potentially serious, embolic complications. **—alan z. segal**

Preoperative Facial Nerve Electrodiagnostic Studies in CP Angle Surgery

ABSTRACT & COMMENTARY

Source: Wedekind C, et al. *Muscle Nerve* 2000;23:1868-1871.

Intraoperative electromyographic (emg) monitoring of facial muscles may be of benefit during surgery in the cerebellopontine angle. Preoperative testing of the facial nerve in these circumstances often reveals various abnormalities of uncertain prognostic value. Are these latter studies necessary?

Prior to the surgical removal of unilateral acoustic neuroma diagnosed by magnetic resonance imaging (MRI), 24 patients, 12 men and 12 women ages 38-68 years, underwent electrodiagnostic studies to determine their value in predicting postoperative facial nerve function. Recording from nasalis, studies included transcranial magnetic stimulation of the contralateral facial motor cortex and ipsilateral cisternal portion of the facial nerve, blink reflex study, facial nerve motor evoked response, and F wave studies. Preoperatively, all patients demonstrated clinically intact facial nerve function and all patients were severely hearing impaired. A retrosigmoid suboccipital approach was used for all and diagnosis was histologically verified. Results were analyzed using Student's t-test, Spearman rank correlation coefficient, and P values.

Eleven (45.8%) of the operations resulted in severe or total facial palsy. No significant correlation was demonstrated, in either the early or late follow-up period of up to two years, with any of the electrodiagnostic parameters measured. Only tumor diameter correlated with facial nerve function at three months post surgery. Preoperative electrodiagnostic studies are of no value in predicting facial nerve function following acoustic neuroma surgery.

COMMENTARY

No comment is made in this paper regarding hearing improvement that may have occurred following surgery. In a Japanese series (*Nippon Jibiinkoka Gakkai Kaiho* 1995;98:8-15), among 17 acoustic tumors surgically removed 10 (59%) appreciated useful hearing following

surgery with 13 showing measurably improved audition. Smaller tumor size, sudden onset of hearing loss, and hearing loss of recent onset were clinical predictors of improved hearing postoperatively. For hearing preservation, tumor size (predictably!) and level of preoperative hearing are the significant predictive criteria (*Neurochirurgie* 1997;43:8-14). **—michael rubin**

Muscarinic Agonist Lowers Alzheimer CSF Amyloid

ABSTRACT & COMMENTARY

Source: Nitsch RM, et al. *Ann Neurol* 2000;48:913-918.

Af102b, an investigational cholinergic agonist that binds to the muscarinic M1 receptor, is reported to lower total cerebrospinal fluid beta amyloid levels in Alzheimer's disease (AD) patients. AF102B was previously found to decrease amyloid secretion in cell cultures and to have cognitive enhancing properties in mice and aged rats.

Nitsch and colleagues administered doses up to 80 mg of AF102B three times a day to 19 AD patients of mild to moderate severity. The patients underwent lumbar puncture (LP) at baseline prior to treatment and during four weeks of maximal dosing of AF102B. A separate set of AD patients who were involved in clinical trials of hydrochloroquine and physostigmine also underwent LPs at comparable intervals to the first group. The spinal fluid obtained from all patients was subjected to analysis using an ELISA technique to determine total amyloid beta-protein levels as a surrogate marker of drug effect. Total amyloid beta protein levels are not reported to change substantially over time in untreated AD patients.

The most common side effects of AF102B treatment were gastrointestinal side effects, excessive sweating, and headaches. Among the 19 AD patients treated with AF102B, 14 experienced a decline in total amyloid beta levels, averaging 22% below baseline. In three cases, amyloid beta protein levels increased and two remained unchanged. Among 10 patients receiving hydrochloroquine, amyloid levels increased in five, decreased in two, and were unchanged in three. In the nine patients treated with physostigmine, amyloid levels increased in four, decreased in four, and remained the same in one. The change in average amyloid levels between baseline and maximal treatment were statistically significant in the AF102B-treated group only. Levels of the 42 peptide form of amyloid beta and truncated amyloid precursor protein derivatives did not change significantly in any group.

COMMENTARY

This interesting study forgoes the use of the standard cognitive and functional-based outcome measures usually used in AD clinical trials, and substitutes serial measurements of a surrogate biological marker in the cerebrospinal fluid as the primary outcome measure. Nitsch et al judiciously avoid making any claims of having found a disease-modifying therapy and acknowledge the limitations of using a single marker as a measure of therapeutic efficacy. They also point out that clinical and behavioral measures will be required to judge the value of amyloid-reducing therapies in the treatment of AD.

Unfortunately, the observation of a decrease in total amyloid beta protein levels with AF102B treatment neither proves or disproves that this compound has a positive effect on the AD brain. In the CSF of patients with probable AD, levels of the 42 peptide form of amyloid beta protein are lower than normal, perhaps reflecting sequestration of this peptide in plaques or other deposits in the brain. It is, therefore, unclear whether lowering total amyloid beta levels, while leaving the 42 peptide form unchanged, is a therapeutically positive, negative, or indifferent result. The lack of alteration in amyloid precursor protein derivatives further confounds interpretation of these findings, since these derivatives were altered by the compound in cell culture studies.

We are likely to see more and more use of surrogate biological markers in future studies of putative AD therapies. This study demonstrates the viability of involving patients receiving other investigational therapies as controls and suggests the importance of measuring multiple biological and clinical markers in future studies. It also highlights some of the difficulties ahead in establishing whether potential disease-modifying agents exert positive effects in the treatment of this chronic, complex neurodegenerative disorder. **—norman r. relkin**

Predicting IVIG Response in Multifocal Motor Neuropathy

ABSTRACT & COMMENTARY

Source: Van den Berg-Vos RM, et al. *Ann Neurol* 2000;48: 919-926.

Multifocal motor neuropathy with conduction block (MMNCB) is a progressive, peripheral,

purely motor, multifocal, demyelinating neuropathy resulting in motor weakness, muscle atrophy, and impaired deep tendon reflexes. It responds to intravenous immunoglobulin (IVIG), though not to prednisone or plasmapheresis, but treatment is costly and response is not entirely predictable.

Between 1996 and 1999, 37 patients presenting with a lower motor neuron syndrome and electrodiagnostic evidence of conduction block or demyelination were prospectively studied. By design, none had bulbar signs or symptoms, upper motor neuron signs, sensory deficit on examination, or sensory nerve conduction abnormalities, in keeping with a diagnosis of MMNCB. All underwent extensive electrophysiologic studies, blood work, and IVIG treatment (0.4 g/kg for 5 days) to determine which factors positively predicted response to IVIG in MMNCB. Response was defined as a 50% strength improvement in two or more muscle groups with no muscle group weakening by 25%, as graded by handheld dynamometry and medical research council (MRC) scale. A total of eight muscle groups were defined, encompassing the proximal and distal segment of each limb. Fisher's exact test, the Mann-Whitney U test, stepwise forward logistic regression, and X2 testing were used for statistical analysis.

Clinically positive response to IVIG was significantly associated with younger age at onset (mean age 35.1 ± 9.1 years vs 46 ± 16.3 years), and fewer affected limb regions (3.3 vs 5.1). In the serum, lower creatine kinase levels (< 180 U/L) and elevated anti-GM1 antibodies were positive predictors. Electrophysiologically, definite conduction block (> 50% area reduction over long nerve segments or > 30% amplitude reduction over 2.5 cm segment) and higher distal mean motor amplitude (mean, 7.1 mV vs 5.5 mV) on nerve conduction studies were significantly associated with positive response. Patient gender, disease duration, cerebrospinal fluid protein concentration, and abnormal brachial plexus magnetic resonance imaging (MRI), including nerve swelling or increased signal intensity, were not predictive of response. Response to IVIG in MMNCB may be predicted based on these criteria.

COMMENTARY

In a multicenter efficacy study, 16 patients with MMNCB were randomized into a double-blind, placebo-controlled, crossover trial of IVIG (0.4 g/kg for 5 days; *Neurology* 2000;55:1256-1262). Five patients failed to improve but the remainder had dramatic (n = 9), moderate, or mild (n = 1 each) improvement. In this study, perhaps due to its small size, only younger age predicted positive response, whereas number of affected limbs, abnormal nerve territories, and anti-GM1 titer did not correlate. IVIG is the treatment of choice for surgery.

Accurate prediction of response to MMNCB must await larger series. For now, despite the expense, patients must be given the benefit of the doubt, and therapy initiated. Continuance thereof will depend on clinical response. **—michael rubin**

Dramamine Superior to Lorazepam for Treatment of Acute Vertigo

ABSTRACT & COMMENTARY

Source: Marill KA, et al. *Ann Emerg Med* 2000;36:310-319.

Vertigo is one of the most commonly encountered and difficult to treat complaints in neurologic as well as general practice. A multitude of treatment options may be used, but none are clearly preferred as the agent with an ideal ratio of benefits to side effects. Anticholinergics, benzodiazepines, antihistamines, neuroleptics, and other agents have been used with variable success.

Marill and associates performed a study of 74 patients presenting to the emergency room (ER) with acute vertigo. Patients were prospectively randomized in a double-blind fashion to either intravenous lorazepam (2 mg) or dimenhydrinate (50 mg). The latter agent is available in oral form under the brand name Dramamine. It is a salt of the antihistamine diphenhydramine and 8-chlorotheophylline.

Vertigo was assessed by a 10-point patient rating scale. In a pilot study, vertigo during ambulation was found to be more sensitive than vertigo while lying in bed, sitting, or with head turn. This was, therefore, the primary outcome variable. The severity of vertigo during ambulation was also of practical significance as patients must be able to walk to be discharged from the ER. Secondary end points included symptoms such as nausea, treatment-related sedation, and overall "readiness to go home."

The mean magnitude of vertigo decreased from 6.4 to 2.6 (decrease = 3.8) in the dimenhydrinate group compared with 7.4 to 4.8 (decrease = 2.6) in the lorazepam group—a statistically significant difference. As Marill et al note, patients in the lorazepam group had higher pretreatment vertigo severity. In the overall cohort, however, patients with more severe vertigo benefited more from treatment. This would have biased in favor of lorazepam rather than against it.

Patients treated with lorazepam experienced significantly more sedation. Nausea decreased similarly in both treatment groups. Overall, 32 (86%) patients in the dimenhydrinate groups were "ready to go home" two hours after treatment compared with 25 (69%) in the lorazepam group. This assessment was made variably by the treating physician or the patients, with comparable results by either method.

COMMENTARY

This study was not performed by neurologists. As assessed by ER physicians, the discharge diagnosis assigned to the majority of patients was "acute vertigo," presumably of peripheral origin, rather than a more specific neurological disorder. It is not completely clear how many of the patients had true vertigo as opposed to more nonspecific dizziness. Patients were evaluated for nystagmus (present in > 60%) but not for other neurological signs. As Marill et al acknowledge, central vertigo (e.g., related to brainstem or cerebellar ischemia) probably comprised a negligible fraction of this population of patients (mean age = 45). Indeed, among the minority of patients in whom neuro-imaging was performed (n = 12, primarily CT), only one was positive (a cerebellar infarct). It is possible that patients with central-type vertigo were considered "too sick" for study enrollment or were considered ineligible due to concerns of stroke or TIA. Marill et al do not have specific data regarding these possible exclusions.

Despite these diagnostic considerations and the lack of any placebo-control group (considered unethical by Marill et al), this study is useful and important. An informal poll of neurologists in Marill et al's practice showed that most did not consider Dramamine to be efficacious in their patients with vertigo. Rather, they commonly prescribe benzodiazepines for this purpose. The data from Marill et al suggest that Dramamine, an easily obtained over-the-counter preparation, may be equally or more effective than lorazepam, a schedule II drug that is restricted and has significant abuse potential. **—alan z. segal**

CME Questions

6. All of the following may be symptoms of CSF hypovolemia *except*:
a. nausea.
b. tinnitus and hearing loss.
c. bradykinesia.
d. CSF rhinorrhea.
e. cervical radiculopathy.

7. In the studies on Huntington's disease, five reported cases in each group have reached nine months or longer for evaluation. Which one of the following is *incorrect*?
a. One patient died of cardiac disease after 18 months implantation. At autopsy the implantations showed no inflammation.
b. Although the above patient was implanted in both striata, postmortem study found only one striatum had become functional.
c. In both groups of five patients, four improved at one-year duration.
d. Between the two groups of patients at five years, four improved in one whereas only three improved in the other.

8. Measuring facial motor response by:
a. preoperative transcranial magnetic stimulation of the contralateral facial motor cortex is of value in predicting postoperative facial nerve function following acoustic neuroma surgery.
b. preoperative transcranial magnetic stimulation of the ipsilateral cisternal portion of the facial nerve is of value in predicting postoperative facial nerve function following acoustic neuroma surgery.
c. preoperative blink reflex study is of value in predicting postoperative facial nerve function following acoustic neuroma surgery.
d. preoperative facial nerve motor conduction studies and F-wave studies are of value in predicting postoperative facial nerve function following acoustic neuroma surgery.
e. preoperative tumor size is of value in predicting postoperative facial nerve function following acoustic neuroma surgery.

9. Total amyloid beta levels in spinal fluid:
a. are a diagnostic marker for Alzheimer's disease.
b. provide an accurate measure of beta amyloid levels in the brain.
c. do not change substantially in untreated Alzheimer's patients.
d. are a prognostic marker in Alzheimer's patients.

10. Which factor is *not* of positive predictive value regarding response to intravenous immunoglobulin (IVIG) in multifocal motor neuropathy and conduction block (MMNCB)?
a. Younger age at onset
b. Fewer affected limb regions
c. Lower creatine kinase level (< 180 U/L)
d. Higher cerebrospinal fluid protein concentration
e. Higher distal mean motor amplitude on nerve conduction studies

11. In treatment of acute vertigo, all of the following are true *except*:
a. Dramamine reduces symptoms more than does lorazepam.
b. Lorazepam results in a greater degree of sedation than does Dramamine.
c. Dramamine is superior to lorazepam for vertigo associated with a brainstem or cerebellar insult.
d. No single agent is universally accepted as ideal treatment.

In Future Issues:

Does TPA Damage Brain Cells?