Providing Evidence-based Clinical Information for 21 Years

NEUROLOGY ALERT®

A monthly survey of developments in neurologic medicine

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

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

THOMSON
AMERICAN HEALTH CONSULTANTS

INSIDE

Idiopathic Intracranial Hypertension May Not Be Idiopathic

ABSTRACT & COMMENTARY

Source: Farb RI, et al. Idiopathic intracranial hypertension: The prevalence and morphology of sinovenous stenosis. *Neurology*. 2003;60:1418-1424.

THIS IS AN ELEGANT STUDY, WHICH EXAMINED WHETHER sinovenous obstruction may play a role in idiopathic intracranial hypertension (IIH). Farb and associates carried out studies using elliptic-centric-ordered 3-dimensional gadolinium-enhanced MR venography. This is a very sophisticated and reliable technique for visualizing the venous system. They prospectively studied 29 patients with established IIH as well as 59 control patients. The MRI venography studies were read in a blinded, randomized fashion by 3 readers. A novel scoring system was used to grade the degree stenosis seen in the transverse and sigmoid sinuses of each patient. Farb et al found that there was excellent reproducibility between the 3 readers in the application of the grading system. They observed substantial bilateral sinovenous stenoses in 27 of 29 patients with IIH and only 4 of 59 control patients. They concluded that by using a novel grading system, as well as MR venography for quantifying sinovenous stenoses, that they can identify IIH patients with a sensitivity and specificity of 93%.

■ COMMENTARY

The pathophysiology of elevated intracranial pressure in idiopathic IIH is unknown. Elevated intracranial pressure has been attributed in the past to cerebral venous sinus occlusion, as well as radical neck dissection with removal of the jugular vein. It also, however, occurs in other settings, such as hypoparathyroidism, vitamin A intoxication, systemic lupus erythematosus, and renal disease, as well as being a side effect of a number of medications. Most patients with IIH are young, obese women who present with chronic daily headaches and papilledema. They may not uncommonly have an empty sella. The disease can be associated with transient visual obscurations, pulsatile tinnitus, and eventual visual loss. The neuro-

VOLUME 21 • NUMBER 11 • JULY 2003 • PAGES 81-88

logic signs occasionally include sixth nerve palsies. On rare occasion, IIH can occur without papilledema. Previous authors have suggested that IIH may result from decreased CSF resorption. In a previous study of patients with IIH, 5 of 10 had dural venous outflow obstruction on venography and the other 5 had normal anatomy, while 10 had elevated superior sagittal sinus pressure.

Farb et al have convincingly shown that patients with IIH show venous abnormalities including narrowing. It, therefore, appears that most cases of IIH are at least predisposed to by venous sinus abnormalities and narrowing. This is an extremely interesting observation. It, however, cannot account for all cases of IIH, such as those associated with vitamin A intoxication and some drug reactions. Nevertheless, patients who have these venous abnormalities may be predisposed to interactions with other factors that may modulate CSF production and reabsorption. Unfortunately, although the present study was extremely elegant in showing the venous sinus abnormalities, this technology is not readily available. The present study also does not lead to any new insights about effective treatments for IIH. Nevertheless, the findings are of considerable scientific interest since they provide an explanation for most cases of IIH.

— M. FLINT BEAL

Neurology Alert, ISSN 0741-4234, is published monthly by Thomson 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

Thomson 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.

Congenital Myasthenia and ChAT

ABSTRACT & COMMENTARY

Source: Schmidt C, et al. Congenital myasthenia syndrome due to a novel missense mutation in the gene encoding choline acetyltransferase. *Neuromuscul Disord*. 2003; 13:245-251.

CONGENITAL MYASTHENIC SYNDROMES (CMS) ARE present at birth. Some patients, however, may not seek medical attention until later in childhood or adulthood. Classified as presynaptic, synaptic, or postsynaptic defects, multiple gene mutations have been described. Involvement of the a, b, d, or e subunit of the acetylcholine receptor (AchR) encompasses slow channel syndrome, fast channel syndrome, and AchR deficiency, all postsynaptic defects, as are end plate rapsyn deficiency and end plate acetylcholinesterase deficiency. These latter 2 reside on chromosomes 11p and 3p, respectively. Only recently has a presynaptic mutation been elucidated for CMS.

Three patients from 2 separate kinships were studied, both from Turkey, and both reported consanguinity in the parents. Presentation was neonatally or after age 1 year. In 1, feeding and swallowing difficulties were noted at birth, followed by fatigability in the second year of life. In 2 other children, exercise-induced muscle weakness or ptosis were noted after 1 year. All 3 patients experienced multiple episodes of sudden apnea. Mutation analysis of the choline acetyltransferase (ChAT) gene revealed a single, novel, and identical point mutation in all patients, resulting in the exchange of isoleucine for threonine at codon 336. Unaffected family members either did not carry the mutation or demonstrated only a single allele with the mutation. This was consistent with recessive inheritance. CMS with episodic apnea is the first presynaptic CMS to be genetically elucidated and confirmed.

■ COMMENTARY

CMS should be considered in any patient with a suspected neuromuscular junctionopathy in whom AchR and calcium channel antibodies are negative. Infantile or childhood symptoms and a family history of possible CMS will often be uncovered by a meticulous history. Electrodiagnostic studies and therapeutic response to acetylcholinesterase (AchE) inhibitors will then permit accurate diagnosis in most instances. Repetitive nerve stimulation in CMS reveals a decemental pattern at low

rates (2-5 Hz) of stimulation, similar to that seen in autoimmune myasthenia gravis (MG). Higher rates (10-50 Hz) may also produce a decrement, allowing differentiation of CMS from MG. When rapid repetitive nerve stimulation results in an incremental response, consider congenital Eaton Lambert myasthenic syndrome, which, like episodic apnea, is a presynaptic CMS. Exercise and AchE inhibitors partially or fully reverse the decrement in most CMS, as does 3,4-diamonopyridine. Exceptions to this rule include AchE deficiency and slow channel syndrome. Morphological studies are only rarely required for precise diagnosis. These include electron microscopic examination of the end plate to estimate AchR number and AchE amount and microelectrode studies to assess end plate potentials and quantal release of Ach. Peripheral blood DNA analysis for molecular genetic testing is available for diagnostic confirmation when indicated. **— MICHAEL RUBIN**

AD Vaccine Alters Disease and Pathology in Humans

ABSTRACTS & COMMENTARY

Sources: Nicoll JA, et al. *Nat Med*. 2003;9(4):448-452; Hock C, et al. *Neuron*. 2003;38:547-554.

TWO RECENT REPORTS STRONGLY SUGGEST THAT Elan's AN-1792 Alzheimer's "vaccine," which was withdrawn from clinical trials after several Alzheimer's disease (AD) patients developed severe brain inflammation, did in fact succeed in altering the course of AD in some cases.

Nicoll and colleagues from Southampton, UK, reported the postmortem findings from a 72-year-old woman with AD who developed brain inflammation after multiple injections with AN-1792 and died 12 months after her last injection. On postmortem analysis of the brain, large areas of the neocortex were found to have very few senile plaques, in contrast to the persistence of other elements of AD-associated pathology, such as neuropil threads, tangles, and amyloid angiopathy in the same areas. This pattern strongly resembles that observed in the brains of AD-model transgenic mice treated with AN-1792. Signs of a T-cell-mediated meningoencephalitis were also found. This is consistent with previous reports that the adverse inflammatory effects of AN-1792 are T-cell mediated, whereas the therapeutic effects are likely brought about by B cells. The findings suggest that immunotherapy can reduce the burden of amyloid-bearing plaques from the human brain.

In a study of a subset of patients involved in the Elan trial, investigators in Zurich found that 20 of 30 subjects injected at their site raised significant titers of anti-amyloid antibodies. Among those with a robust antibody response, the scores on tests of memory, general cognition, and daily function declined significantly less than in the subjects who failed to raise high titers of antibody. Benefits were seen in 2 of 3 patients who developed the meningoencephalitis transiently as a result of immunization. This study suggests that high titers of antibodies after immunization with AN-1792 can be associated with decreased progression of AD symptoms.

■ COMMENTARY

Taken together, these 2 reports imply that a major landmark has been reached in the history of research on AD treatment. Although the data must be considered preliminary, there are strong indications that amyloid immunotherapy exerted a disease-modifying effect in humans, manifested by altered brain pathology, as well as a measurable symptomatic response in patients raising high antibody titers. Although injections of AN-1792 have been suspended, additional follow-up is being carried out on those already injected, and more information about treatment response should become available in the near future. Alternatives to AN-1792 that may be less prone to cause inflammatory side effects are under development, as are other methods of altering amyloid processing. These studies provide some of the first concrete evidence that a new generation of disease-modifying therapies for AD is on the way. **— NORMAN R. RELKIN**

Determinants of Survival in Patients with Vertebrobasilar Diseases

ABSTRACT & COMMENTARY

Source: Qureshi AI, et al. Stroke-free survival and its determinants in patients with symptomatic vertebrobasilar stenosis: A multicenter study. *Neurosurgery*. 2003;52:1033-1040.

INTRACRANIAL BALLOON ANGIOPLASTY AND STENT placement now are available to patients suffering from intracranial stenosis that involves the vertebrobasilar arteries (VBA). At present, however, no consensus exists regarding the role of endovascular procedures vs

best medical management. Accordingly, it is imperative to know the natural history of patients affected with posterior circulation intracranial stenosis in order to determine whether the benefit of endovascular treatment outweighs the risks.

Qureshi and colleagues performed a multicenter retrospective study to identify the long-term stroke-free survival of medically treated patients who presented with TIA or stroke related to intracranial VBA stenosis. VBA stenosis was diagnosed on the basis of magnetic resonance angiography and/or conventional angiography.

A total of 102 patients (55 men and 47 women) with TIA (n = 30) or ischemic stroke (n = 72) were included. Their mean age was 64 ± 12 years. The mean period of follow-up was 15 months (range, 1-60 months). During the follow-up period, 14 patients suffered recurrent strokes and 21 died. Sixteen of the deaths were related to initial or recurrent strokes. Stroke-free survival was 76% at 12 months and 48% at 5 years. The risk of recurrent stroke was 11% per year, and the rate of recurrent stroke and/or death was 24% per year. The high mortality probably was due to the severe neurological deficits associated with brainstem strokes that led to fatal complications such as pneumonia and sepsis. Older patients had a decreased stroke-free survival. Treatment with either antiplatelet agents in 41% or warfarin in 32% improved stroke-free survival.

Qureshi et al concluded from these results that further studies are needed to evaluate medical and endovascular treatment options for this group of patients with a poor prognosis for stroke-free survival.

■ COMMENTARY

The 11% annual stroke recurrence rate found by Qureshi et al compares to that reported by the Warfarin-Aspirin for Symptomatic Intracranial Disease (WASID) study group.[1] The WASID investigators studied 59 patients with 50-99% stenosis involving the VBA. Stroke rates in the same territory as the stenotic artery were 11% in patients with basilar artery stenosis and 8% in patients with vertebral artery stenosis. A prospective, randomized study by the WASID investigators has now undertaken to compare the efficacy of aspirin with that of warfarin in preventing recurrent stroke in patients with symptomatic intracranial stenosis.[2] The WASID study will provide prospective data on the prognosis of symptomatic intracranial vascular disease in patients treated with either 1300 mg of aspirin daily or warfarin to achieve an INR of between 2 and 3. Nevertheless, the current study emphasizes the need for a randomized comparison of current best medical therapy with the latest endovascular techniques and intracranial stents. It is hoped that such a study will show that endovascular techniques produce not only improved vascular patency and restored blood flow but also greater patient well-being. **— JOHN J. CARONNA**

References

1. The Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) study group. *Stroke*. 1998;29:1389-1392.
2. Benesch CG, Chimowitz MI. *Neurology*. 2000;55: 465-466.

A New Risk Factor for Cardiovascular Disease

ABSTRACT & COMMENTARY

Source: Shishehbor MJ, et al. Association of nitrotyrosine levels with cardiovascular disease and modulation by statin therapy. *JAMA*. 2003;289:1675-1680.

THIS IS A STUDY THAT EXAMINED LEVELS OF nitrotyrosine, a specific marker for protein modifications produced by nitric oxide-derived oxidants. Shishehbor and associates studied plasma levels in patients with coronary artery disease (CAD) and determined whether they are modulated by treatment with a HMG CoA-reductase inhibitor (statins). They carried out a case control study and an interventional at 2 tertiary care referral centers. In the case control study, 100 case patients with established CAD and 108 patients with no clinically evident CAD were recruited consecutively. In the interventional study, patients with hypercholesterolemia underwent nutrition and exercise counseling, or when cholesterol levels failed to decrease within 6-8 weeks they were enrolled for 12 weeks to receive 10 mg daily of oral atorvastatin therapy. Thirty-five patients participated in this phase of the trial. Shishehbor et al found that nitrotyrosine levels were significantly higher among patients with CAD. The overall value is 9.1 μmol/mol of nitrotyrosine/tyrosine vs 5.2 μmol/mol in the controls. Patients in the upper quartile of nitrotyrosine had higher odds of CAD as compared to those in the lowest quartile within an adjusted odds ratio of 6.1. The upper quartile of nitrotyrosine levels remained associated with CAD after correction for CRP levels as well as the Framingham Global Risk Score. Statin therapy reduced nitrotyrosine levels significantly by 25%. This was similar in magnitude to the reductions in total cholesterol levels, which were also 25%. This, however, was

independent of any changes in lipoproteins or inflammatory markers such as CRP.

■ **COMMENTARY**

These findings are of considerable interest. They provide direct evidence that oxidative damage to lipids may play a critical role in the pathogenesis of atherosclerosis. This may be true of both CAD and stroke. There previously has been substantial evidence for nitrotyrosine immunostaining in atherosclerotic plaques. The present report, however, is the first to correctly demonstrate a correlation between plasma levels of nitrotyrosine and risk of CAD. It is of considerable interest that statin treatment significantly reduced the levels of nitrotyrosine. This most likely is due to its anti-inflammatory effects. This suggests that the beneficial effects of statin treatment may be dependent not only on its ability to lower cholesterol but also on its anti-inflammatory activity. Interestingly, the increases in nitrotyrosine appear to be independent of traditional CAD risk factors and CRP levels. Altogether the findings suggest that nitrotyrosine measurements may prove useful in assessing CAD status and for monitoring the anti-inflammatory effects of statins. **— M. FLINT BEAL**

Talk More, Examine Less

ABSTRACT & COMMENTARY

Source: Dooley JM, et al. The utility of the physical examination and investigations in the pediatric neurology examination. *Pediatr Neurol*. 2003;28:96-99.

In this original study, 500 consecutive pediatric referrals for neurologic consultation were assessed to determine what influence, if any, was played by the history, neurologic examination, and investigations, with respect to final diagnosis and patient management. Upon receipt of a referral letter, the consulting neurologist was asked to predict what he or she would find on examination, what the final diagnosis would be, and what testing might be necessary. Upon seeing the patient, the neurologist was blinded to the previous predictions and, after obtaining the history and once more after the examination, opinions were again sought with respect to the final diagnosis and need for investigations. Data were analyzed using EPI Info version 6.04b, a microcomputer word-processing, database, and statistics program for epidemiology.[1]

Final diagnoses for the 500 children included headache (n = 150), seizures (n = 68), Tourette syndrome (n = 58), attention-deficit-hyperactivity disorder/learning disability (ADHD/LD) (n = 41), cerebral palsy (n = 21), developmental delay (n = 18), or other neurologic disorders (n = 144). Among headache patients, Tourette syndrome, ADHD/LD, and developmental delay, the neurologic examination never influenced management or outcome. Examination was influential in 4 patients each with seizures or cerebral palsy. Investigations never influenced Tourette syndrome, ADHD/LD, or cerebral palsy but did influence management or outcome in 16 seizure patients. Investigations were rarely useful in developmental delay, where only 1 suspected fragile X was found to have normal chromosomal analysis, or in headache referrals, where in only 2 patients other disorders were excluded by imaging and/or EEG. Neither examination nor investigations influenced Tourette syndrome or ADHD/LD. For the majority of pediatric neurology consultations, most efforts should be expended on history, by far the singular critical component to appropriate patient care.

■ **COMMENTARY**

The underpinnings of the neurologic examination can be traced back to antiquity. Herophilus and Eristratus (ca 280-290 BCE), of Alexandria, Egypt, first mention the cranial nerves, though it was left for Rufus of Ephesus (ca 100) to note that they and the brain constituted an anatomic continuum. Galen of Pergamon (d 216) authored 15 volumes titled *On Anatomic Procedures*, identifying 10 pairs of cranial nerves, at least 1 incorrectly. Thomas Willis (1621-1675) correctly labeled 6 pairs, but it was Samuel Thomas von Soemmering (1755-1830) who classified 12 cranial pairs, later formalized in 1895 with the publication of *Basle Nomina Anatomica*. [2]

Gowers elegantly outlined the orderly examination of the motor system in 1886 with publication of his *Manual of Diseases of the Nervous System*, incorporating the concept of an upper and lower motor neuron with notation of their different signs.[3] Earlier, Erb and Westphal had simultaneously introduced deep-tendon reflexes to the medical literature, with Erb correctly interpreting the phenomenon as representing a true reflex arc.[4] Dysdiadochokinesis was coined by Babinski in 1902, while rebound was described by Gordon Holmes in 1904, who also described dysmetria in 1917. These components of the cerebellar examination were soon incorporated into contemporary textbooks of neurology and included in the neurologic examination.[5] Brown-Sequard, Edinger, Rinne, and van Gehuchten, among others, contributed to elucidating the anterolateral, pain and temperature, and posterior, vibration, and position sensory pathways.

Steeped though it is, in the ancient past, the neurologic examination is not yet ready for the ashbin of history. However, as managed care evolves, its cost-effective delivery will likely demand that we take Dooley and associates' results into consideration in the not-too-distant future. Further confirmation of these findings, with their extension into adult counterparts, will be welcome.
— MICHAEL RUBIN

References

1. Dean AG, et al. CDC. Atlanta, GA. 1977.
2. Steinberg DA. *Semin Neurol*. 2002;4:349-356.
3. York GK. *Semin Neurol*. 2002;4:367-374.
4. Louis ED. *Semin Neurol*. 2002;4:385-390.
5. Fine EJ, et al. *Semin Neurol*. 2002;4:375-384.

Early Axonal Injury in Multiple Sclerosis

ABSTRACT & COMMENTARY

Source: Filippi M, et al. Evidence for widespread axonal damage at the earliest clinical stage of multiple sclerosis. *Brain*. 2003;126:433-437.

FILIPPI AND COLLEAGUES PERFORMED CONVENTIONAL brain MRIs and whole-brain N-acetylaspartate (WBNAA) measurements with proton magnetic resonance spectroscopy in 31 patients presenting with clinically isolated syndromes suggestive of multiple sclerosis (MS). This was compared with 16 normal controls. Patients were rescanned by conventional MRI 4-6 months later to detect dissemination of lesions in time. The average WBNAA concentration was significantly lower ($P < .0001$) in this early MS population (10.09, SE 0.43) compared to controls (12.98, SE 0.58). The reduction in WBNAA in MS patients did not correlate with other brain MRI parameters, such as gadolinium enhancement, T2 lesion load, brain atrophy, or dissemination of lesions. Based on this 20% reduction in WBNAA in early MS patients, Filippi et al concluded that axonal and neuronal injury occurs early in the course of MS, somewhat independent of the more obvious MRI measurements.

■ COMMENTARY

It is unclear what such sensitive measures of WBNAA at early stages of MS truly reflect about brain pathology (ie, axonal transection with cell death vs impaired neuronal physiology with mitochondrial dysregulation). Some simple questions were not addressed in this study. How did WBNAA measures vary over time? How were they affected by corticosteroid or interferon-beta treatment? Are WBNAA changes seen in "pure" spinal or optic nerve forms of demyelination (ie, the monosymptomatic transverse myelitis or optic neuritis patient)? If WBNAA measures are obtained on "normal" individuals with a strong family pedigree for MS, what is the earliest discernable alteration that can be detected—perhaps many years before more obvious clinical or paraclinical measures evolve? It remains to be seen what this sensitive brain spectroscopy measure clearly reflects about early brain pathology in MS, but it supports the concept of early treatment intervention.
— BRIAN R. APATOFF

Tightening the Belt on Hypertension

ABSTRACT & COMMENTARY

Source: Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). US Department of Health and Human Services. NIH Publication No. 03-5233. May 2003.

HYPERTENSION IS A MAJOR RISK FACTOR FOR BOTH ischemic and hemorrhagic stroke. This and other risk factors for atherosclerosis are not merely issues for middle and late age. These are processes that begin early in life and cause cumulative damage to small and large arteries supplying the brain and within the brain. The recently released JNC 7 report is, therefore, of great importance to neurologists interested in stroke prevention.

The JNC report identifies "pre-hypertension" for individuals with blood pressures > 120 systolic or 80 diastolic (*see Table*). Although not recommended for antihypertensive medications, these BP goals mandate lifestyle modifications for a huge number of Americans previously not thought to be at increased risk. Lifestyle modifications include weight reduction, diet modifica-

Table

Blood pressure category	Systolic	Diastolic
Normal	< 120	< 80
Prehypertension	120-139	80-89
Hypertension, Stage 1	140-159	90-99
Hypertension, Stage 2	> 160	> 100

tion (low salt, low fat), aerobic exercise, and moderation of alcohol consumption. For those with Stage 1 or 2 hypertension, single-drug regimens may be insufficient, and there should be a low threshold for dual therapy (such as with an ACE inhibitor and a diuretic). Patient blood pressures should be aggressively checked at office visits, by outpatient BP monitors and by patient self checks.

■ **COMMENTARY**

Untreated hypertension is an epidemic in this country. These new JNC guidelines further magnify this problem. It is incumbent upon neurologists and all health care professionals to educate our patients and encourage crucial lifestyle and pharmacologic interventions. **— ALAN Z. SEGAL**

GBS and GM1b Antibody

ABSTRACT & COMMENTARY

Source: Ogawara K, et al. Anti-GM1b antibody is associated with acute motor axonal neuropathy and *Campylobacter jejuni* infection. *J Neurol Sci*. 2003;210:41-45.

ANTI-GANGLIOSIDE PERIPHERAL NERVE ANTIBODIES IN Guillain-Barré syndrome (GBS) include GM1, asialo-GM1, GQ1b, GD1a, and GT1a. GM1 is associated with pure motor GBS and with the acute motor axonal variant of GBS. GM1b is also associated with GBS, but often its role in the disease is obscured by the concomitant presence of GM1. The role of GM1b in the absence of GM1 remains to be defined.

Among 86 consecutive GBS patients (mean age, 38 years), 24 had both GM1 and GM1b antibodies, whereas 10 each had either GM1 or GM1b antibodies but not both. Of the 10 GM1b-positive/GM1-negative patients, 4 each also demonstrated either GD1a or GalNAc-GD1 antibodies, and 1 showed multiple other antibodies including GD1a, GD1b, GQ1b, and GT1b. None had GM2 antibody activity. Of the 10 GM1b-positive/GM1-negative patients, 60% had *Campylobacter jejuni* infection, 50% had a diarrheal prodrome, and 80% had a diagnosis of acute motor axonal neuropathy (AMAN) with no sensory loss. One patient was unclassifiable electrodiagnostically, and 1 demonstrated changes typical for acute inflammatory demyelinating polyneuropathy on nerve conduction studies. Peak clinical disability and incidence of slow recovery did not differ among those who were GM1b-positive/GM1-negative and those GM1b-negative/GM1-positive. Like GM1, GM1b may be a target neural antigen in AMAN following *C jejuni* infection.

■ **COMMENTARY**

Separation of GM1 antibody into immunoglobulin (IgG) subclasses (IgG1 to 4) suggests that a correlation exists between the particular IgG subclass on one hand and the clinical profile and recovery pattern on the other.[1] Among 42 patients with GM1-antibody-positive GBS, the most frequent subclasses present were IgG1 (n = 32, 76%) and IgG3 (n = 13, 31%). Four patients demonstrated positivity for both IgG1 and IgG3. IgG4 was not seen in any patient; IgG2 was positive in 2 (5%). *C jejuni* serologic positivity and preceding gastrointestinal symptomatology (56% and 63%, respectively) were more common with the former, while antecedent respiratory infection was associated with the latter (77%). No correlation was found between IgG subclass and age, sex, GM1 antibody titer, or median nerve motor potential amplitude. Excluding patients with both IgG1 and IgG3, inability to walk independently at 1, 3, and 6 months following disease onset was more likely in IgG1-positive patients, although nadir disease severity was similar in both IgG1 and IgG3 groups. IgG3 patients were more likely to appreciate rapid recovery, defined as improving by 2 or more Hughes grades from nadir, within the first month of illness. Among GM1-antibody-positive patients, those with the IgG3 subclass of GM1 were more likely to fare better.

How does GM1 antibody mediate its pathogenicity? Sera from 24 GBS patients was obtained to study its ability to influence leukocyte functions including degranulation and phagocytosis.[2] Anti-GM1 antibody-negative serum served as controls. Sixty-seven percent (10 of 15) and 53% (8 of 15) of GM1 antibody-positive sera were able to induce white cell degranulation and phagocytosis, respectively, whereas none of the control sera had such effect. Activation of leukocyte inflammatory functions may be the mechanism of GM1 antibody activity in GBS patients. **— MICHAEL RUBIN**

References

1. Koga M, et al. *Neurology*. 2003;60:1514-1518.
2. van Sorge NM, et al. *Ann Neurol*. 2003;53:570-579.

CME Questions

Effective with this semester, 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.***

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.

1. **Congenital myasthenic syndrome with episodic apnea:**
   a. is a postsynaptic disorder.
   b. results from mutation of the ChAT gene.
   c. AchE inhibitors are of no therapeutic benefit.
   d. electrodiagnostic studies are usually normal.
   e. None of the above

2. **In patients with symptomatic intracranial vertebrobasilar stenosis, the annual rate of recurrent stroke is approximately:**
   a. 2%.
   b. 5%.
   c. 11%.
   d. 15%.
   e. 24%.

3. **In the pediatric population, the neurologic examination is likely to be most useful for the diagnosis or management of which one of the following diagnoses?**
   a. Tourette syndrome
   b. ADHD/LD
   c. Headache
   d. Developmental delay
   e. Seizures

4. **Which of the following is *false*?**
   a. WBNAA changes occur early in MS.
   b. WBNAA levels are increased in MS patients.
   c. WBNAA is a measure of neuronal and axonal function.
   d. WBNAA did not correlate with gadolinium activity on conventional brain MRI.

5. **Among Guillain-Barré syndrome patients:**
   a. GM1b anti-ganglioside antibody does not play a role in disease pathogenesis.
   b. the IgG3 subclass of GM1 antibody is associated with a worse prognosis.
   c. GBS patients positive for GM1 antibodies most often have the IgG2 subclass of GM1.
   d. IgG4 is the most common subclass seen in GM1-positive GBS patients.
   e. None of the above

Answers: 1(b); 2(c); 3(e); 4(b); 5(e)

In Future Issues:

Poliomyelitis and Flaviviruses of West Nile Virus Infection