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NEUROLOGY ALERT®

A monthly survey of developments in neurologic medicine

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Amyloid Vaccine for Alzheimer's?

ABSTRACT & COMMENTARY

Source: Schenk D, et al. Immunization with amyloid-beta attenuates Alzheimer-disease-like pathology in the PDAPP mouse. *Nature* 1999; 400:173-177.

Extraordinary findings by researchers at elan pharmaceuticals suggest the possibility that immunization with beta-amyloid could be effective in treating and preventing Alzheimer's disease. In an unprecedented approach, Schenk and colleagues studied the effects of injecting the 42-peptide form of human beta-amyloid protein into transgenic mice (PDAPP) that overexpress the human-mutant-amyloid-precursor protein (APP). These mice typically develop several features of Alzheimer-like pathology, including amyloid plaques, degenerating neurites, and astrogliosis within one year of birth. In initial experiments, amyloid injections were begun during the first six weeks of life and continued monthly until the mice were 1 year of age. Control PDAPP animals developed extensive amyloid deposits in multiple brain regions over this period. Mice injected with beta-amyloid had nearly complete absence of amyloid deposits in their brains and, likewise, they lacked dystrophic neurites and astrogliosis in most cases.

Schenk et al next evaluated whether immunization with beta-amyloid would affect neuropathological findings if initiated after a substantial burden of plaques already existed in the brain. In this case, they began injections at 11 months of age and continued for either four or seven months. Quantitative image analysis was used to measure alterations in amyloid burden relative to control animals receiving injections of a nonamyloid compound. The control mice exhibited a 17-fold increase in brain beta-amyloid burden from 12-18 months of age while beta-amyloid-injected animals had a 99% reduction in amyloid burden over a comparable period. Both diffuse and mature amyloid deposits were reduced in the beta-amyloid-immunized mice and remaining plaques often stained positive for IgG. The other elements of Alzheimer-like pathology present in this mouse model, such as neuritic dystrophy and astrogliosis, were also significantly reduced by beta-amyloid immunization.

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In explaining their results, Schenk et al cite the considerable body of evidence indicating that a chronic inflammatory state exists in the brains of patients with Alzheimer's disease, and suggest that augmenting the specific immune response to beta-amyloid may prove beneficial in preventing and treating the disorder in humans.

COMMENTARY

Although medical science usually moves forward in small, logical steps, major advances are occasionally wrought by conceptual leaps of faith. The very idea that generating a specific peripheral immune response would significantly alter Alzheimer's neuropathology within the immunologically privileged confines of the blood-brain barrier seemed sufficiently far-fetched to deter most investigators from even considering this approach until now. Having obtained this fortunate outcome in young transgenic mice, Schenk et al pressed on to see what effect they might have on older animals with already established neuropathological changes. A reasonable expectation might have been that immunization would arrest subsequent plaque development without affecting existing deposits. Once again, expectations were violated as Schenk et al carefully documented a substantial reduction in both the total amyloid burden and other features of Alzheimer-like pathology. In total, these findings are so unexpected that their credibility almost certainly would have been doubted were they the work of less accomplished and respected scientists.

Many tantalizing questions remain to be addressed. The most pressing issues are whether a vaccine based on beta-amyloid could be safely used in humans and if this treatment will have the desired effect on the development and progression of Alzheimer's disease. One safety concern relates to the constitutive expression of beta-amyloid throughout the body that could lead to an autoimmune response to a vaccine based on the human protein.

Accepting that these results will be replicated in other transgenic animal models, the applicability of these findings to the human disease remains in question. Overproduction of a mutant form of beta-amyloid is known to be pathologically relevant to a small number of early-onset familial cases of Alzheimer's associated with possession of specific autosomal dominant mutations. Although several lines of evidence point to a central role for beta-amyloid in the more commonly occurring forms of Alzheimer's disease, it is unclear whether interventions affecting amyloid clearance in PDAPP mice will prove applicable to human patients lacking this mutation. Furthermore, the PDAPP mice (indeed, all of the existing amyloid-based transgenic models) lack key elements of human Alzheimer's pathology, particularly neurofibrillary tangles. In several other neurodegenerative disorders, tangles develop in the absence of senile plaques. This makes it conceivable that an intervention that prevents, or even reverses, amyloid deposition may still not cure the disease.

The only way to satisfactorily answer these questions is to test this approach in human patients. Before human trials can be initiated, technical issues concerning the appropriate choice of adjuvants and avoidance of autoimmune responses must be addressed. This approach is likely to be fast-tracked for human trials by both the pharmaceutical company and federal regulatory agencies in light of the far-reaching implications of these animal studies. Although it may be several years before safety and efficacy are established, many interesting neurobiological questions should be answered in the process of testing this extremely exciting and unexpected new inroad to Alzheimer's therapy. **—nrr**

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

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GST Registration Number: R128870672.
Second class postage paid at Atlanta, GA.
POSTMASTER: Send address changes to ***Neurology Alert,*** P.O. Box 740059, Atlanta, GA 30374.

Back issues: $33. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

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Subscription Prices

United States
$209 per year (Student/Resident rate: $100).

Multiple Copies
1-9 additional copies: $100 each. 10 or more copies: $60 each.

Outside the United States
$229 per year plus GST (Student/Resident rate: $110 plus GST).

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Thymectomy for the Elderly Myasthenic

ABSTRACT & COMMENTARY

Source: Tsuchida M, et al. Efficacy and safety of extended thymectomy for elderly patients with myasthenia gravis. *Ann Thorac Surg* 1999;67:1563-1567.

Among 94 patients who underwent thymectomy for myasthenia gravis (MG) between 1985 and 1996, comparison between those older (n = 69) and younger (n = 25) than 60 years of age was performed to determine and contrast safety and efficacy of the procedure in these two groups. Diagnosis was based on clinical signs and symptoms, positive edrophonium test, and electromyography, and indications for surgery included generalized and ocular MG under maximum medical therapy. All patients underwent transsternal thymectomy and postoperative management included anticholinesterase agents and corticosteroids as needed. Outcome was evaluated at one year or more postoperatively and scored as remission, improvement with the same or less medication, same symptoms with more medication, or worse. Statistical analysis used the X^2 test and P less than 0.05 was considered significant.

Although the two groups differed significantly regarding thymic pathology postoperatively, with hyperplasia more common in the young (45% vs 16%) and thymoma in the old (40% vs 32%), preoperative data, apart from age, did not differ between the groups. Remission was more likely in the young (40% vs 8%; P < 0.05) but improvement, worsening, or death occurred equally in both groups. Thymectomy was of benefit in 97% and 83% overall in the young and old, respectively. Older age is not a contraindication to thymectomy in MG, and improvement requiring continued medication, though not remission, is to be expected.

COMMENTARY

Thymectomy is of demonstrable benefit in the management of MG but a growing literature suggests that it may not be without long-term risks, including the late emergence of autoimmune disorders encompassing systemic lupus erythematosus, Hashimoto's thyroiditis, ulcerative colitis, polymyositis, and primary antiphospholipid antibody syndrome (*N Engl J Med* 1964;278: 229-232; *Neurology* 1979;29:1436-1437; *Acta Neurol Scand* 1992;85:63-65; *Lupus* 1997;6:474-476). To explore the pathophysiology of this association, 16 long-term (> 8 years) post-thymectomy MG patients were compared to six recent (< 1 year) post-thymectomy MG patients, 13 nonthymectomized MG patients, and 32 normal controls (Gerli R, et al. *J Allergy Clin Immunol* 1999;103:865-872). All patients were off immunoactive agents for at least 22 months and only anticholinesterase agents were permitted. Serologic studies were undertaken, encompassing rheumatoid factor, IgG, IgA, and IgM levels, anticardiolipin IgG or IgM antibodies, and thyroid and acetylcholine receptor antibodies. T- and B-cell subtypes were also analyzed, including CD3+, CD4+, and CD8+ T cells, and CD19+, and CD19+/CD5+ B cells, as well as the Vb T-cell receptor repertoire of CD4+ and CD8+ cells comprising Vb2, Vb3, Vb5a, Vb5b, and Vb6a. Follow-up of MG patients was undertaken for three years to ascertain the development of autoimmune disorders, and statistical analysis of the results used one-way ANOVA comparison.

Significantly reduced numbers of T cells, with normal CD4+/CD8+ ratio, and expansion of natural killer CD16+/CD57- cells characterized the long-term post-thymectomy group. Total and CD5+ B cells were normal but IgG, IgM, anticardiolipin, and anti-dsDNA antibodies were increased, and ANA titre of 1:160 or more were only seen in this group. Two long-term patients, but none in the other groups, developed autoimmune disease, one with lupus and one with undifferentiated connective tissue disease. T-cell lymphopenia and hypergammaglobulinemia are seen long-term post-thymectomy and these long-term effects may explain the development of autoimmune disease in MG as a consequence of thymectomy rather than as an association of autoimmune disease with MG ab initio. **—mr**

Myasthenia, Thymectomy, and Prognostic Predictors

ABSTRACT & COMMENTARY

Source: Nieto IP, et al. Prognostic factors for myasthenia gravis treated by thymectomy: Review of 61 cases. *Ann Thorac Surg* 1999;67:1568-1571.

To determine prognostic indicators influencing outcome following thymectomy for myasthenia gravis (MG), Nieto and colleagues reviewed the clinical records of 61 MG patients, 23 men and 38 women, who, between 1977 and 1994, underwent transsternal (n = 58) or transcervical (n = 3) thymectomy with complete excision of the thymus and neighboring fat tissue. Most were Osserman grade IIa

(n = 19) or grade IIb (n = 38), mild or moderate generalized MG, respectively, with two each in grade I (ocular) and III (acute fulminant MG). None was grade IV, severe-late MG. Preoperative treatment comprised anticholinesterase agents (AA) in 25, AA and corticosteroids (C) in 16, AA and C and plasmapheresis (PE) in seven, C in five, AA and PE in six, and PE alone in two, whereas postoperative treatment included AA and/or C as needed. Outcome was measured as complete remission, significant clinical improvement requiring medication, moderate clinical improvement requiring medication, no change, or clinical worsening, and statistical analysis included univariate and multivariate analysis using the Cox stepwise regression model.

Over a follow-up period of eight months to 6 years, 29 patients achieved complete remission, and 28 and four patients, respectively, achieved significant or moderate clinical improvement. Mean age was 30 and 45 years for those who did and did not achieve complete remission, but neither this nor gender or thymic pathology influenced complete remission rate. Stage of disease and length of illness prior to surgery were the only significant prognostic indicators, with complete remission associated with surgery within eight months of diagnosis (P = 0.03), and stage I and III patients more likely to achieve complete remission (P = 0.029). No operative mortality was seen in this group and eight suffered postoperative complications, including wound infection, pneumonia, pneumothorax, pleural effusion, or mediastinitis. Early thymectomy is the key to successful treatment of MG (*see Commentary, p. 3*). **—mr**

The Value of MEG in Evaluating Patients for Epilepsy Surgery

ABSTRACTS & COMMENTARY

Sources: Lamusuo S, et al. [18-F]FDG-PET and whole-scalp MEG localization of epileptogenic cortex. *Epilepsia* 1999; 40(7):921-930; Wheless JW, et al. A comparison of magnetoencephalography, MRI, and V-EEG in patients evaluated for epilepsy surgery. *Epilepsia* 1999;40(7):931-941.

Magnetoencephalography (meg) noninvasively records the magnetic fields produced by electrical brain activity and offers a noninvasive method to localize brain function. Previously almost exclusively a research tool, MEG is increasingly used clinically to localize normal and abnormal cortical activity prior to brain surgery. One of the earliest clinical applications of MEG was to localize the origin of epileptic spikes. Unlike the electric fields recorded by conventional electroencephalography (EEG), neuromagnetic fields detected by MEG pass through the skull and scalp undistorted. MEG can localize focal neural activity with a spatial resolution of a few millimeters. The early MEG instruments, however, had few detectors and required repeated measurements for a complete examination. Early MEG studies were time consuming and impractical for routine clinical use. The advent of new MEG systems able to record simultaneously from a large area of scalp, or even from the entire scalp, reduces the time necessary for examination and increases the efficiency of MEG. The clinical use of current MEG systems in the presurgical evaluation of patients with medically intractable epilepsy is the subject of two recent studies by Lamusuo and colleagues and Wheless and colleagues.

Wheless et al prospectively compared surgical outcome in 58 consecutive patients with complex-partial seizures with the location of epileptogenic regions predicted by MEG, MRI, surface EEG, and subdural EEG. For each method, Wheless et al applied a "concordance" scale that characterized the overlap of the predicted epileptogenic region(s) by each method and the region resected at surgery. Surgical outcome was used to rate each method by whether a predicted epileptogenic region hit, partially hit, or missed the clinical goal of seizure relief. Overall, taking both patients with temporal and extratemporal resections, ictal subdural EEG hit in 69% of patients, and MEG hit in 52%. By comparison, interictal subdural EEG (48% hits), ictal and interictal surface EEG (32% and 44% hits, respectively), and MRI (48% hits) did no better than MEG. There was no statistically significant difference between methods. In the subgroup of patients with extratemporal resections, MEG achieved 44% hits, compared to 81% and 75% hits for ictal and interictal subdural EEG, a statistically significant difference in favor of subdural EEG. Once again, the surface EEG and MRI did no better than MEG. In summary, in this series of 58 patients with complex-partial seizures, a single MEG study identified an epileptogenic region of cortex as well as continous surface EEG recordings that required inpatient hospitalization.

Currently, the routine presurgical evaluation of epileptics usually includes high-resolution brain MRI, ictal surface EEG, and, frequently, positron emission tomography (PET). It is possible that a combination of noninvasive methods, such as MEG, MRI, and PET, can reduce or

eliminate the need for prolonged inpatient surface EEG monitoring. Lamusuo et al studied nine epileptic patients who were undergoing evaluation for epilepsy surgery and who, by surface EEG, had either extratemporal epilepsy or poorly localized seizure onset. They compared the information obtained by MEG, [18F]-fluorodeoxyglucose PET (FDG-PET), and subdural EEG, and surgical outcome in operated patients' recordings to ascertain the consistency in information provided by each method. Of nine patients, six underwent surgery. Outcome was best in five surgical patients where MEG and FDG-PET results agreed. These patients either became seizure free (n = 2), had rare seizures (n = 1), or had a more than 80% reduction in seizures (n = 2). In one surgical patient, MEG and FDG-PET results disagreed. This patient received no benefit from surgery. Of the patients who did not have surgery, two had concordant MEG and FDG-PET findings that identified regions of eloquent cortex that were unresectable. One patient had bilateral epileptic foci on MEG and subdural EEG, and did not receive surgery. MEG and FDG-PET, however, did not identify the same regions as subdural EEG in every instance. In one patient, MEG and FDG-PET did not detect an extratemporal focus seen by subdural EEG, while in another patient, MEG and FDG-PET identified an extratemporal focus that was not seen on subdural EEG. In short, this study by Lamusuo et al offers a case series in which best results following epilepsy surgery were achieved in cases where MEG and FDG-PET data agreed.

COMMENTARY

These studies illustrate the imperfect state of presurgical assessment for epilepsy surgery. Even invasive intracranial monitoring predicted outcome (hits) in only 69% of patients. For this reason, the assessment for epilepsy surgery relies on various methods of assessment. The data presented by Wheless et al include only those patients who had surgery, so no statement can be made of the relative value of MEG in predicting which patients would not benefit from surgery. Nevertheless, these results place MEG in a similar predictive category as ictal and interictal EEG monitoring, which is the mainstay of the initial presurgical evaluation. The other major diagnostic modality used for presurgical evaluation is FDG-PET. To this end, the study by Lamusuo et al, though limited by the small number of patients, is both encouraging and cautionary. Combining FDG-PET with MEG evaluation holds the promise of identifying those patients who may benefit from epilepsy surgery, or at least from intracranial EEG monitoring. However, Lamusuo et al present evidence that MEG and FDG-PET may not detect regions of seizure onset seen by subdural EEG, and may also detect regions not seen on SD-EEG. The importance of this underinclusion or overinclusion of epileptogenic foci can only be determined through correlation with surgical outcome. To this end, there is a need for the clinical study of sufficient patients with FDG-PET and MEG to determine if this combination of noninvasive tests successfully predicts clinical outcome better than current methods. The cost of MEG is another factor that will determine its clinical use. At present, the fee for a study ranges from $1000-5000, and the cost of an MEG instrument is similar to an MRI machine. If, as these studies hint, an MEG study is clinically equivalent to inpatient surface EEG monitoring, the cost of one MEG study compares favorably with the cost of hospitalizing a patient for continuous EEG monitoring. Until the clinical applications of MEG expand, however, the high installation cost of MEG will restrict the technology to research centers and epilepsy referral centers that handle a large number of patients. **—fl**

Twelve-Month Follow-Up of t-PA Treated Patients

ABSTRACT & COMMENTARY

Source: Kwiatkowski TG, et al. Effects of tissue plasminogen activator for acute ischemic stroke at one year. *N Engl J Med* 1999;340:1781-1787.

The ninds recombinant tissue plasminogen activator (t-PA) Stroke Study (The NINDS rt-PA stroke study group. *N Engl J Med* 1995;333:1581-1587) found that patients treated with t-PA within three hours after the onset of acute stroke symptoms were 30% more likely than placebo controls to have minimal or no disability three months later. Mortality at three months among t-PA patients (17%) was similar to that of controls (21%), despite the higher frequency of symptomatic intracerebral hemorrhage (6%, 50% fatal) in the t-PA group.

The present study confirmed that the magnitude of benefit (30% with an absolute increase in favorable outcome of 11-13%) persisted in the t-PA-treated group at six and 12 months. No significant difference in mortality affected treated (24%) vs. control patients (28%; P = 0.29). There was no detectable association between the type of stroke identified at baseline and 12-month outcome. The rate of recurrent stroke at 12 months was 5% in both groups.

COMMENTARY

This follow-up study validates the valuable effect imposed by thrombolytic therapy with t-PA given within three hours after stroke onset both immediately and permanently. The results contrast with the negative or equivocal findings of European trials of thrombolytic agents given up to six hours after the onset of stroke symptoms (MAST-I Group. *Lancet* 1995;346:1509-1514; The Multi-Center Acute Stroke Trial—European Study Group. *N Engl J Med* 1996;335:145-150; Hacke W, et al. *Lancet* 1998;352:1245-1251).

Kwiatkowski and associates found that t-PA benefitted all subgroups of ischemic strokes. Consequently, they again advise against selection of patients for t-PA treatment based on the presumed mechanism of stroke. In addition, certain variables such as younger age, lower NIH stroke score, and absence of diabetes at baseline were associated with a favorable outcome and survival at 12 months. Since none of these variables interacted with treatment, they should not influence selection of patients for t-PA treatment.

Thrombolytic treatment with t-PA remains the first-line therapy for acute ischemic stroke patients regardless of stroke subtype. **—jjc**

Pain Management for the Elderly and Terminally Ill

ABSTRACT & COMMENTARY

Source: Carver AC, et al. End-of-life care: A survey of US neurologists' attitudes, behavior, and knowledge. *Neurology* 1999;53:284-293.

Medical science and care since the end of World War II has brought out an astounding number of medications, specific disease therapies, and novel surgical procedures. The work of Carver and colleagues has resulted in extending the mature and, especially elderly, lives of a large percentage of the U.S. population. Antihypertensives, cardiac surgery, anticancer therapy, renal transplants, and novel pharmacologic drugs have all contributed to the success. On the down- side, however, one finds a substantial increase in the incidence of irreversibly demented patients in nursing homes, patients suffering excruciating pain as they encounter the painful dwindling benefits of chemotherapy, and the terror that affects persons with late amyotrophic lateral sclerosis (ALS) as the disease deprives them of their ability to breathe, speak, or even gesture.

Against this background, the American Academy of Neurology surveyed the opinions of 600 randomly chosen neurologists, 250 neuro-oncologists, and 149 ALS specialists, not all neurologists. Two specific questions were addressed: 1) Would you participate in doctor-assisted suicide (e.g., to give a fatal dose of morphine)?; or 2) Would you assist in voluntary euthanasia (e.g., by intentionally giving the patient a fatal dose of drugs both of which would be at the patients' request)? Although 95% of the respondents reported that advanced directives would ease the decision process of withdrawing life-sustaining treatment when needed, only about 30% of their patients had provided advanced directives. Most important was that only 18% of doctors endorsed providing advanced medication sufficient to produce suicide at a subsequent date. Ninety-four percent of the respondents indicated that they would provide palliative care with morphine, but only 21-25% with consent would give a morphine dose large enough to kill even the most agonized patient. However, if physician-assisted suicide with firm constraints became legal, 70-75% of reporters indicated that chronic, severe, intolerable pain would be an appropriate reason for responding to pleas for physician-assisted suicide. Under present laws, about 13% of neurologists would participate in physician-assisted suicide and only 4% would prescribe in advance sufficient drugs for the patient to commit suicide. What is really troublesome, however, is that less than 50% of respondents indicate that even when legally protected they would not participate in either physician-assisted suicide or the patients' voluntary euthanasia. (*See Brief Alert, "Pain: Mechanisms and Treatment," p. 7.*)

COMMENTARY

Figures similar to the above are expressed by many other groups of doctors in this country, irrespective of their disciplines. Nevertheless, distinguished physicians and surgeons in the past have quietly recognized that patients suffering non-remediable, agonizing, protracted and incurable pain must be relieved even if fatal doses of analgesics were the only solution. It is true that recent Supreme Court decisions have an ambiguity that merely indicates that assisted suicide is not an individual's constitutional right (Burt RA. *N Engl J Med* 1997;337:1234-1239). Nevertheless, in a subtle but unquestionable way, the court accepts terminal patient-demanded euthanasia delivered by lethal levels of sedation. This obviously opens a wide door of potential activity in which palliative management no longer relieves the patient's suffering.

The puzzle is that in many other medical disciplines, less than 50% of the members would provide euthanasia

even if the law directly supported the act. The reaction must be more than just doubt that the patient might recover. Why have more than 50% of doctors resisted the ultimate treatment for irreversible, increasing, prostrating pain? Is it a religious principle? If so, that conflicts with the patient's constitutional rights. Is it because they fear prosecution for the action? Ethical committees can help to solve this quandary. I strongly favor palliative treatments for pain that can restore a patient's well-being for as long as possible. But when palliation is totally against the wall of improving, how will this 50% serve their patients? **—fp**

Brief Alerts

Pain: Mechanisms and Treatment

Sources: Carr DB, Goudas LC. Acute pain. *Lancet* 1999; 353:2051-2058; Cervero F, Laird JM. Visceral pain. *Lancet* 1999;353:2145-2148; McQuay H. Opioids in pain management. *Lancet* 1999;353:2229-2232; Chapman CR, Gavrin J. Suffering: The contributions of persistent pain. *Lancet* 1999; 353:2233-2237.

Pain is one of the most frequent symptoms brought to physicians and, especially, neurologists. Anesthesiologists have brought important, temporary treatment to the problem, but neither general nor regional anesthesia scores high in the management/treatment of chronic pain. Neurologists, despite their considerable contact with patients suffering chronic pain, have given only limited attention to increasing new knowledge about both new and chronic pain, as well as their different pathways to successful management. The *Lancet*, published in London and increasingly carrying information reports relevant to clinical neurology, has recently devoted 10 successive articles addressing new knowledge about pain mechanisms and their management. Starting with an overview of pain responses (Loeser JD, Melzack R. *Lancet* 1999; 353:1607-1609) and their neurobiology (Besson JM. *Lancet* 1999;353:1610-1615), the series proceeds with the following weekly informative chapters: cancer pain (Portenoy RK, Lesage P. *Lancet* 1999;353:1695-1700); assessment of patients' reporting pain (Turk DC, Okifuji A. *Lancet* 1999;353:1784-1788); chronic pain management (Ashburn MA, Staats PS. *Lancet* 1999;353:1865-1869); and neuropathic pain (Woolf CJ, Mannion RJ. *Lancet* 1999;353:1959-1964). **—fp**

Oxygen for Carbon Monoxide Poisoning

Source: Scheinkestel CD, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: A randomized controlled clinical trial. *Med J Aust* 1999;170:203-210.

Your editor, not having direct access to the original journal, presents here its critical points as summarized by the *American College of Physicians Journal Club* (*ACP J Club* 1999;131:11). The gist of the extraction is that of 191 patients with carbon monoxide poisoning, 104 were randomized to hyperbaric oxygen (HBO) at 2.8 atmospheres for 100 minutes × 3 days, whereas 87 patients were placed in the chamber and inhaled 100% oxygen at 1.0 atmosphere following the previous protocol. Patients who remained severely damaged repeated the pressure/atmosphere procedure for three extra

treatments. All patients underwent a battery of seven neuropsychologic tests after they recovered to a reasonable steady state. Although more HBO patients had more second round treatments than the NBO group, differences in the groups' ultimate neuropsychologic scores did not differ from each other except that the NBO group had better scores than the HBOs in auditory verbal learning.

COMMENTARY

Your editor has long doubted the value of HBO in this setting. Small one-person pressure chambers have been placed entrepreneurially in the United States and, without scientific trial, recommended for improving outcome from asphyxia, brain trauma, or stroke. Indeed, the state of Florida actually reimburses the costs of these gadgets without any scientific evidence of their specific therapy. It's time for neurologists to develop strong and ethical neurological rehabilitation centers based on strong scientific underpinnings, lest evermore dubious and expensive devices raise rehabilitation costs. **—fp**

Aspirin for Carotid Endarterectomy

Source: Taylor DW, et al. Low-dose and high-dose acetylsalicylic for patients undergoing carotid endarterectomy: A randomised, controlled trial. *Lancet* 1999;353:2179-2184.

Taylor and colleagues found that 2849 patients randomized for endarterectomy taking 81 or 325 mg of aspirin had a significantly (P = 0.002 [30 days] or P = 0.0002 [3 months]) lower risk of stroke, myocardial infarction, and death than did patients taking 650 mg or 1300 mg of the drug. The outcome speaks for itself. **—fp**

CME Questions

15. Injections of beta-amyloid into transgenic mice bearing Alzheimer-like pathology:

a. cause a fatal autoimmune response.
b. decrease amyloid burden but not other Alzheimer-like pathology.
c. decrease amyloid burden, astrogliosis, and neuritic dystrophy.
d. have no measurable effect on brain pathology.

16. Which of the following statements is correct?

a. Older age is not a contraindication to thymectomy in myasthenia.
b. Complete remission following thymectomy in myasthenia is most likely when surgery is performed late in the disease.
c. Stage IV myasthenia patients are more likely than stages I-III to achieve complete remission following thymectomy.
d. T-cell lymphopenia is seen short-term post-thymectomy in myasthenia.
e. Hypergammaglobulinemia is seen long-term in nonthymectomized myasthenic patients.

17. At baseline, which of the following can be used to select patients for t-PA treatment?

a. Absence of diabetes mellitus
b. Age younger than 55 years
c. Embolic stroke
d. Atherothrombotic stroke
e. None of the above

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In Future Issues: Movement Disorders