For patients with symptomatic or asymptomatic carotid artery stenosis, the combined risk of stroke, MI, or death does not differ significantly between carotid artery stenting and carotid endarterectomy.

Background: Results of the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) are available.

Objective: To compare carotid artery stenting (CAS) with carotid endarterectomy (CEA) for symptomatic and asymptomatic carotid artery stenosis.

Design: Multicenter, randomized, controlled trial.

Participants: 2522 patients with carotid stenosis were randomized to either CAS or CEA. The 1262 CAS patients included for data analysis were not different at baseline from the 1240 CEA patients (age, approximately 69 years; males, 64% to 66%; asymptomatic, 47%; and ≥70% stenosis, 85% to 87%). Approximately 85% of both groups had hypertension and/or hyperlipidemia, and about 26% of both groups were smokers. Subjects were considered symptomatic if they had transient ischemic attacks or minor stroke in study artery territory <180 days before randomization. Eligibility criteria included stenosis ≥50% on angiography, ≥70% on ultrasound, or ≥80% on CTA or MRA, with ultrasound revealing 50% to 69% stenosis. Exclusion criteria included prior severe stroke, chronic atrial fibrillation (AF), recent paroxysmal AF, anticoagulation, unstable angina, and recent myocardial infarction (MI).

Methods: The RX Accunet embolic-protection device was used >96% of the time. Approximately 90% of CEAs were performed under general anesthesia. Antiplatelet therapy was begun before intervention: CAS subjects received dual antiplatelet therapy for at least 4 weeks; and CEA subjects were treated with a single drug (91% post-CEA). Perioperative clinical status, cardiac enzymes, and ECGs were monitored. Carotid ultrasonography was performed before the procedure, at 1, 6, and 12 months afterward, then annually. Follow-up telephone interviews were conducted at 3 months and every 6 months thereafter. Follow-up was performed up to 4 years (median, 2.5 years). Primary outcome end point was stroke, MI, or death from any cause during the peri-procedural period or ipsilateral stroke within 4 years.

Results: The 4-year rate of stroke or death was 6.4% with stenting and 4.7% with CEA ($P = 0.03$). This difference appeared to be due to peri-procedural complications, with no significant difference between CAS and CEA for peri-procedural death (0.7% vs 0.3%), but significant differences between the 2 groups for stroke (CAS, 4.1% vs CEA 2.3%; $P = 0.01$) and MI (CAS, 1.1% vs CEA, 2.3%; $P = 0.03$). After this period, the incidence of ipsilateral stroke with stenting and CEA were not significantly different (2.0% vs 2.4%). The 4-year composite end point rates of stroke or death among symptomatic subjects were 8.0% and 6.4%; rates among asymptomatic subjects were 4.5% and 2.7% (not significant).

Conclusions: For patients with symptomatic or asymptomatic carotid stenosis, the combined risk of stroke, MI, or death did not differ significantly between CAS and CEA. During the peri-procedural period, there was a higher risk of stroke with stenting and a higher risk of MI with CEA.

Reviewer's Comments: It is unclear whether some or all stenting subjects continued dual antiplatelet therapy for the duration of the study. Restenosis rates were not reported for the treatment groups. The long-term natural history of carotid artery stents still appears to be unknown. (Reviewer-W. Steven Metzer, MD).

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Keywords: Carotid Stenosis, Endarterectomy, Ischemia, Vascular Stent, Embolic Protection

Print Tag: Refer to original journal article
Brain Stimulation May Help Patients With Aphasia

Using Transcranial Direct Current Stimulation (tDCS) to Treat Stroke Patients With Aphasia.

Baker J, Rorden C, Fridriksson J:

Stroke 2010; 41 (June): 1229-1236

Noninvasive brain stimulation coupled with intensive language therapy is a promising new approach to improve language function in patients with aphasia after stroke.

Background: Anodal transcranial direct current stimulation (A-tDCS) is a safe and noninvasive modality to stimulate cortical areas of the brain.

Objective: To determine if A-tDCS stimulation of the left frontal hemisphere improves naming ability in patients with aphasia due to stroke.

Participants: 10 subjects with aphasia were included. All subjects had one isolated left hemispheric stroke >6 months previously. In addition, subjects were <85 years of age, were right handed before the stroke, were native English speakers, and had participated in a previous functional MRI study of aphasia.

Interventions: The stimulation protocol consisted of 5 consecutive days of A-tDCS at 1 mA for 20 minutes. The site of stimulation of the intact left frontal lobe was determined for each patient based on activation patterns on functional MRI during a naming task.

Methods: Concurrent with the electrical stimulation, subjects underwent a standardized anomia treatment, which utilized a computerized self-administered word/picture matching task. As a control, subjects also underwent computerized anomia treatment with sham brain stimulation. The outcome of interest was naming performance, involving both words that were encountered as part of the anomia treatment and words that were not encountered. Subjects were tested at baseline, again after 5 days of treatment, and then 1 week after discontinuation of treatment.

Results: Patients experienced improved naming ability during the A-tDCS, which persisted for 1 week after completion of therapy. Naming also improved with sham stimulation, but there was a statistically significantly greater improvement with active stimulation compared to sham stimulation. Naming improved for both words presented during the computerized training sessions and for untested words. There was a wide variation in the degree of improvement, with those having non-fluent aphasia or a lesion proximate to the area of stimulation demonstrating a greater benefit. Patients tolerated the stimulation well, with minimal side effects.

Conclusions: A-tDCS coupled with intensive language therapy may be a useful approach to improve naming ability in patients with chronic stroke.

Reviewer’s Comments: In this small study, a-tDCS was shown to improve naming ability when coupled with anomia treatment in patients with aphasia after stroke. There is tremendous excitement in the neuro-rehabilitation field about new technologies that may allow clinicians to enhance the neurophysiological processes that mediate stroke recovery. More studies are needed to see if these new modalities are indeed safe and effective. In addition, important parameters such as the timing and duration of treatment, the intensity of stimulation, and the optimum location to stimulate still need to be determined. This study adds to the body of literature suggesting that we may soon be able to intervene in the natural history of stroke and enhance the recovery process. (Reviewer-Aninda B. Acharya, MD, MSPH).

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Keywords: Stroke, Rehabilitation, Aphasia

Print Tag: Refer to original journal article
Patients exhibiting a vegetative state at 1 year after coma onset either die or remain vegetative over the next 5 years. In contrast, patients in a minimally conscious state at 1 year improve in about one third of cases, but disability remains severe.

**Background:** Clinical misdiagnosis of the vegetative state (VS) is common (up to 40%), because physicians miss instances when brain-injured patients display fragments of awareness or interact minimally with the environment. These patients are more appropriately classified as exhibiting a minimally conscious state (MCS). They may be able to reach for objects, visually fixate, repeat a single word, or gesture to a command. Approximately 70% emerge from the MCS in 1 to 3 months after coma onset. When MCS is prolonged, however, the outcome is unclear.

**Objective:** To compare the long-term (5-year) outcome of patients diagnosed with VS versus MCS at 1 year after coma onset.

**Methods:** Retrospective clinical review of the records of 12 VS and 39 MCS patients. Outcomes were assessed at 2, 3, 4, and 5 years after injury by the Glasgow Outcome Scale plus an additional category for patients in MCS. The relationships between each outcome and 10 predictor variables were examined by a logistic regression analysis. Four of the predictor variables involved auditory-evoked potentials taken early in the coma.

**Results:** Among the 12 VS patients, 9 (75%) died, 2 remained vegetative, and 1 was lost to follow-up. Among the 39 MCS patients, 14 (36%) died, 9 (23%) remained in MCS, and 3 were lost to follow-up. The other 13 MCS patients (33%) improved. They answered yes/no verbally or through a head/hand/eyes communication code and produced isolated words; 60% showed functional object use. The best outcome patients (n=4) spoke in simple sentences, regained partial ambulation, helped in activities of daily living, and lived at home with assistance. All 13 patients were cognitively impaired. Improvement occurred primarily in the second year but was also seen in subsequent years. Of those with improvement, 70% were traumatic brain injury (TBI) patients. Predictors of poor outcome included a diagnosis of VS, age >39 years, and bilateral absence of cortical components of middle-latency auditory-evoked potentials.

**Conclusions:** No VS patient improved during the follow-up period. In contrast, one third of MCS patients showed improvement >1 year after coma onset. For prognostic purposes, the authors emphasized the need to distinguish MCS from VS by careful, periodic re-evaluations and suggested that early auditory-evoked potentials could be useful.

**Reviewer's Comments:** Physicians must search for the presence of awareness in behavioral responses in VS patients. No matter how subtle or transient the response, its presence indicates a diagnosis of MCS and not VS. Early improvement (between 1 and 3 months after coma onset) occurs in 70% of MCS patients. The current study shows that improvement in MCS continues for years in a decreasing minority of cases and depends heavily on the type of injury. MCS individuals who suffered TBI stand a much better chance of late improvement than MCS patients with ischemic-hypoxic brain damage after cardiac arrest. (Reviewer-Michael Jacewicz, MD).

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Keywords: Vegetative State, Minimally Conscious State, Coma Prognosis

Print Tag: Refer to original journal article
Are Labor and Delivery Complications Worse in Mothers with Stroke?

Stroke During Pregnancy: No Increased Risk of Preterm Delivery and Low Birth Weight, A Nationwide Case-Controlled Study.

Kang J-H, Lin H-C:

J Neurol Neurosurg Psychiatry 2010; May 16 (): epub ahead of print

Pre-eclampsia/eclampsia, anemia, and gestational hypertension are associated with stroke during pregnancy.

Background: Numerous changes occur in a woman during pregnancy, involving coagulation, vascular reactivity, hormonal status, and volume shifts. These are thought to be associated with the rare complication of stroke during pregnancy.

Objective: To investigate factors associated with stroke during pregnancy, and to explore the frequency and risk for adverse pregnancy outcomes in a Chinese population.

Methods: The study used the Taiwan National Health Insurance Research Dataset, which includes the majority of the Taiwanese population. It also used the national birth certificate registry, which includes both infant and parents' birth dates, gestational week at birth, birth weight, gender, parity, place of birth, parenteral educational level, and maternal marital status. All women with a live singleton birth over a 3-year period were included. If a mother had >1 pregnancy, only the first was included. Women with any type of stroke before pregnancy were excluded. A comparison group of 8 age-matched normal subjects for every stroke patient were randomly selected from the remaining normal pregnancies. The independent variable was whether a woman had a stroke during pregnancy. Dependent variables included low birth weight, preterm gestation, and small for gestational age (SGA; gestational age-specific birth weight <10th percentile). Characteristics of the mother (age, educational level, and marital status), infant (gender and parity), family monthly income, and comorbid medical disorders (gestational hypertension, gestational diabetes, anemia, and hyperlipidemia) were adjusted for.

Results: 473,529 women had live singleton births, of whom 272 had a diagnosis of stroke. After exclusions, 161 mothers with stroke during pregnancy were included; 1288 mothers without stroke were randomly selected and age matched to those with stroke. Family monthly income was significantly lower in those who had a stroke than in those who did not. Women who suffered a stroke were also significantly more likely to have comorbidities of gestational hypertension and anemia. There were no significant differences in maternal level of education, marital status, or infant gender or parity. In addition, there were no significant differences in the prevalence of preterm births, low-birth-weight infants, or SGA infants between mothers with or without strokes. Mothers with stroke were more likely to have pre-eclampsia/eclampsia than were mothers in the comparison group. No significant differences were found in the risk of complications of labor and delivery between the 2 groups.

Conclusions: There was no statistically significant difference in pregnancy outcomes between Chinese women with stroke during pregnancy and those without.

Reviewer's Comments: This study shows that there is no major morbidity or mortality of infants born to mothers with stroke during pregnancy. Recent studies have shown generally good infant outcomes after thrombolytic therapy, antiplatelet medications, and cesarean deliveries in mothers with stroke during pregnancy. (Reviewer-John Schwankhaus, MD).

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Keywords: Stroke, Pregnancy, Gestational Hypertension, Pre-Eclampsia, Eclampsia, Anemia

Print Tag: Refer to original journal article
In patients with reversible cerebral vasoconstriction syndromes, posterior reversible encephalopathy syndromes and ischemic stroke are especially likely when MRA shows combined vasoconstriction of the proximal middle and posterior cerebral arteries.

**Objective:** To investigate the evolution of vasoconstriction on magnetic resonance angiography (MRA) in patients with reversible cerebral vasoconstriction syndromes (RCVS).

**Participants:** 77 patients met the following diagnostic criteria: diffuse severe headache of abrupt or progressive onset with or without focal neurological deficits or seizures; "strings and beads" appearance on MRA and subarachnoid hemorrhage ruled out by appropriate investigations; headache that develops simultaneously with neurological deficits or seizures; and headache and neurological deficits that resolve spontaneously within 2 months.

**Methods:** Patients received nimodipine immediately upon confirmation of diagnosis, except for those with spontaneous resolution of headache before presentation. Measurement of vasoconstriction on MRA was based on a formula that included the stenosed diameter and the diameter of the vessel proximal to the stenotic site. First and second segments of the anterior, middle, and posterior cerebral arteries and the basilar artery were measured. Follow-up MRA examinations were conducted until normalization of vasoconstriction or for 6 months.

**Results:** Of 77 patients, 69 were women. The mean age was 48 years, with a range of 10 to 76 years. Systolic blood pressure during headache attacks ranged from 101 to 220 mm Hg; 17% of patients had pre-existing migraine. Associated conditions included the use of a selective serotonin reuptake inhibitor or pseudoephedrine, an unruptured saccular aneurysm, vertebral artery dissection, postpartum state, and microangiopathic hemolytic anemia. Patients had an average of 7 thunderclap attacks (range, 2 to 30) in a mean of 17 days (range, 5 to 42 days). The mean number of arterial segments involved on initial MRA was 5.3. Vasoconstriction score reached maximum at roughly the same time that headaches resolved, namely between 16 and 17 days after headache onset. Seven patients developed posterior reversible encephalopathy syndromes (PRES), and 6 had ischemic stroke. A combined score for middle cerebral artery first segment and posterior cerebral artery second segment was associated with the highest risk of PRES (OR, 11.6) and ischemic stroke (OR, 3.4). Two patients had permanent visual field defects at 3-month follow-up.

**Conclusions:** The severity of vasoconstriction on initial MRA has prognostic value in RCVS and can guide management.

**Reviewer's Comments:** The symptoms of RCVS can be indistinguishable from subarachnoid hemorrhage, but vasoconstriction in RCVS tends to be more widespread and involve shorter segments. Angiographically, RCVS may be difficult to distinguish from primary angiitis of the nervous system, but thunderclap headache would be unusual in that condition. (Reviewer-John C. Brust, MD).

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Keywords: Reversible Cerebral Vasoconstriction, Magnetic Resonance Angiography

Print Tag: Refer to original journal article
The diagnosis of normal pressure hydrocephalus is based on the classical symptoms of "magnetic" gait impairment, urinary incontinence, and cognitive impairment.

**Background:** Normal pressure hydrocephalus (NPH) remains a difficult subject for most neurologists. Diagnosis depends on imprecise criteria, and, other than shunt response, there is no gold standard upon which to depend. Some experts advocate predicting shunt response using complicated CSF infusion tests; others suggest a trial lumbar puncture (LP) to assess for gait improvement.

**Objective:** To evaluate shunt responsiveness in relation to the presence and severity of the pathological findings of Alzheimer's disease (AD) in cortex biopsies performed at surgery for placement of ventriculoperitoneal (VP) shunt.

**Design:** Prospective cohort study.

**Participants:** 37 patients aged 50 to 79 years with idiopathic NPH who underwent VP shunting.

**Interventions:** All patients underwent VP shunting via a right frontal burr hole.

**Methods:** Cortical biopsies were processed for light microscopy, stained with the usual methods to identify neuritic plaques, amyloid, and neurofibrillary tangles. Immunostaining was done with antibodies to beta amyloid, TDP 43, phosphorylated tau, and alpha synuclein. AD pathology was scored on a semi-quantitative scale. The diagnosis of NPH was made based on the presence of 2 of 3 classical symptoms: a "magnetic" gait impairment (not further defined), urinary incontinence, and/or cognitive impairment. All conditions had to be progressive. Patients also had to have ventriculomegaly in excess of generalized atrophy, with an Evans index >0.3. History, data, and imaging all had to be consistent with published guidelines for the diagnosis of NPH. Curiously, demonstration of normal CSF pressure at LP and CSF examination were not required. Preoperative and postoperative evaluations included history, neurological exam, cognitive evaluation, and a 15-point quantitative NPH scale, which scored gait, cognition, and continence. There was also a separate gait scoring system. Shunt responsiveness was defined as an improvement of ≥2 points on this 15-point scale.

**Results:** Of the 37 patients enrolled, 25 had some Alzheimer pathology, and 6 had congophilic angiopathy; there was no other cerebrovascular pathology. Among 30 patients followed up long term, 8 had moderate-to-severe AD, 14 had mild AD, and 8 had no changes. Only 2 of 8 patients with moderately severe AD changes improved, while 18 of 22 with mild or no pathology improved. Those with AD in cortical biopsies had more severe impairments at baseline.

**Conclusions:** If AD pathology could be assessed before shunting in patients with suspected NPH, for example, using Pittsburgh B PET scans, patient selection might be improved.

**Reviewer's Comments:** Little is mentioned on complications. There was one death in the 37 patients beginning the study. Nearly 20% of the patients were lost to follow-up. The findings in this paper are at odds with others using similar sample sizes, which noted no effect of cortical AD pathology on shunt responsiveness. However, the neuropathological evaluation in this paper was more complete, as these authors subdivided AD cases into degrees of severity. (Reviewer-James W. Schmidley, MD).

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Keywords: Normal Pressure Hydrocephalus, Alzheimer's Disease, Ventriculoperitoneal Shunt

Print Tag: Refer to original journal article
Apathy and depression in patients receiving subthalamic deep brain stimulation for Parkinson's disease reflect mesolimbic dopaminergic denervation

**Objective:** To study the occurrence, predictors, and mechanisms of apathy after subthalamic nucleus deep brain stimulation (DBS) in patients with Parkinson's disease.

**Participants/Methods:** 63 patients received subthalamic nucleus DBS. All patients had Parkinson's disease with severe levodopa-related motor complications, and all subjects were <70 years of age. Patients with presurgical apathy or moderate-to-severe depression were excluded. Dopaminergic drugs were discontinued on the day of surgery and then reinstated at the lowest dose permitted by the patients' motor state. Monthly assessment for apathy and depression was based on standardized scales. Dopaminergic medication was increased in patients who developed apathy or depression. PET using [11C-raclopride] and methylphenidate stimulation was performed in selected patients who developed apathy and in some who did not in order to compare dopaminergic synapses in selected brain regions.

**Results:** Apathy developed in 34 of the 63 patients between 3 and 8 months of DBS and was reversible in half of these by the 12-month follow-up. Seventeen patients developed depression between 3 and 9 months of DBS. All but one patient was in the apathy group, and depression was transient in all subjects, with a maximum duration of 4 months. A predictor of apathy was presurgical fluctuation in depression and apathy scores. Pathological hyperdopaminergic behaviors, including behavioral addictions, were present in one third of the patients at baseline and disappeared in all patients during follow-up. Preoperative motor state or level of reduction of dopaminergic medication did not predict apathy. In patients who developed apathy, PET studies suggested increased dopamine D2/D3 receptor density, reduced synaptic dopamine level, or both in orbitofrontal, dorsolateral prefrontal, posterior cingulate, and temporal cortices bilaterally, as well as striatum on the left and amygdala on the right.

**Conclusions:** Apathy and depression can occur after DBS as a delayed dopamine withdrawal syndrome associated with mesolimbic dopaminergic denervation. It is plausible that, in contrast to pulsatile pharmacologic treatment, nonpulsatile DBS causes progressive desensitization and disappearance, not only of levodopa-induced dyskinesias but also of ON-period hyperdopaminergic behavior, "unmasking the hypodopaminergic face of the disease."

**Reviewer's Comments:** In addition to clarifying pathophysiological mechanisms underlying these non-motor features of Parkinson's disease, this study has obvious clinical relevance, not the least of which is regarding reports of an increased risk of suicide in patients receiving DBS. (Reviewer-John C. Brust, MD).

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Keywords: Parkinson's Disease, Apathy, Subthalamic Nucleus Stimulation, Dopamine, Depression, Anxiety

Print Tag: Refer to original journal article
The addition of entacapone to levodopa treatment can cause peak-dose dyskinesias.

**Background:** When added to levodopa, the decarboxylase inhibitor, carbidopa, shifts metabolism to the COMT pathway. Clinical improvement is seen in Parkinson disease (PD) patients after adding the COMT inhibitor, entacapone, to levodopa/carbidopa.

**Objective:** To study the effects of the enzyme inhibitors, entacapone and carbidopa, on levodopa concentrations in the blood and CSF.

**Participants/Methods:** 5 PD patients with end-of-dose wearing-off effect were included in the study. Their regular anti-Parkinsonian medications were stopped the night before the study. An intradural catheter was placed in the lumbar region, and 2-mL samples were collected every hour for 12 hours. A microdialysis probe was placed in a brachial vein, with 30 mL collected every 30 minutes for 12 hours. A catheter was placed in the opposite arm for levodopa infusion. On day 1, patients received levodopa 30 mg/hour as an intravenous infusion during the 12-hour period. During day 2, the same dose of levodopa was given in addition to entacapone 200 mg orally just after baseline samples were collected and at 4 and 8 hours into the infusion. On day 3, the same dose of levodopa was given with carbidopa 25 mg added to the 4- and 8-hour entacapone dosages. The differences in the maximum concentration ($C_{\text{max}}$) values between the days were calculated. The area under the concentration time-curve (AUC) was calculated by linear trapezoidal summation to time.

**Results:** One patient was excluded on day 1 due to technical failure. The mean levodopa concentrations increased with the addition of entacapone alone and in combination with carbidopa. There was a similar increase in levodopa concentrations in both the blood and CSF. The mean difference of the $C_{\text{max}}$ levels in the CSF was 11% with the addition of entacapone and 121% with the addition of both entacapone and carbidopa. The corresponding $C_{\text{max}}$ differences in the blood were 33% and 183%, respectively. There was an increase in the AUC with the addition of entacapone to levodopa, and an even bigger increase when both entacapone and carbidopa were added.

**Conclusions:** The addition of entacapone to levodopa treatment yields an increase in the levodopa concentration with an increased $C_{\text{max}}$ for levodopa. This is seen in both the CSF and blood and is more pronounced when entacapone is combined with carbidopa.

**Reviewer’s Comments:** Peak dose dyskinesias and the “on-off” phenomenon are thought to possibly result from a nonphysiological, pulsatile stimulation of the dopamine receptors due to the short half-life of levodopa. Entacapone was thought to possibly help prevent these complications, as it was believed to increase the AUC without increasing the $C_{\text{max}}$ of levodopa. This study casts doubt on the ability of entacapone to prevent dyskinesias. (Reviewer-John Schwankhaus, MD).

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Keywords: Levodopa, Entacapone, Carbidopa

Print Tag: Refer to original journal article
Background: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an autoimmune disease that targets myelin sheaths of peripheral nerves. Clinical evidence supports the efficacy of treating CIDP with a corticosteroid, plasmapheresis, or IV immunoglobulin (IVIg). A multicenter, randomized double-blind study published in 2008 and 2009 confirmed the efficacy of IVIg for CIDP (IVIg for the Treatment of CIDP: the ICE study), with 54% of subjects responding to IVIg (vs 21% responding to placebo) within 24 weeks. The ICE study investigators now report on the timing, course, and clinical characteristics of response to IVIg for CIDP.

Objective: To investigate the timing, clinical course, and clinical characteristics of response to IVIg for patients with CIDP.

Design: Extraction of data from a multicenter, randomized double-blind study.

Participants: 117 patients with CIDP in the ICE study were diagnosed by accepted clinical and neurophysiological diagnostic criteria; 59 of these were treated with IVIg. Of these, 32 (54%) were identified as responders and comprised the study group for this investigation.

Methods: Patients with CIDP were randomized to treatment with IVIg or placebo. IVIg-treated subjects received 2 g/kg over 2 to 4 days, then 1 g/kg every 3 weeks for up to 24 weeks. Responders were defined as subjects who received IVIg and had a positive change in score on the Inflammatory Neuropathy Cause and Treatment scale.

Results: In the ICE trial, 54% of CIDP subjects responded to treatment with IVIg versus 21% of subjects treated with placebo ($P < 0.001$). Only 14 of these 32 responders (24% of the treated cohort) improved within 3 weeks. An additional 16 patients (27%) responded to IVIg treatment by week 6 of treatment with IVIg.

Conclusions: Patients with CIDP may require $>1$ treatment with IVIg over 6 weeks to determine if there is a response. Additional treatments may be required to achieve and maintain a maximal clinical response.

Reviewer's Comments: As a clinician, I have always had some uncertainty about what percentage of patients with CIDP respond to IVIg, and when to decide whether or not they have responded to IVIg. This investigation helps to address this problem. The evidence indicates that only about half of patients with CIDP respond to treatment with IVIg, and only about one fourth of these patients respond within 3 weeks. About one fifth of patients get better with placebo. This information should help clinicians in deciding how to treat CIDP patients. (Reviewer-W. Steven Metzer, MD).

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Keywords: Chronic Inflammatory Demyelinating Polyradiculoneuropathy, IV Immunoglobulin

Print Tag: Refer to original journal article
The biologically active form of vitamin D is 1,25 dihydroxyvitamin D, but the major circulating form is serum 25-hydroxyvitamin D.

**Background:** Vitamin D has immunomodulatory properties, generally suppressing pro-inflammatory pathways. The epidemiology of multiple sclerosis (MS) includes a well-known latitude gradient, with risk of MS increasing with latitude north or south of the equator, just as sunlight exposure decreases with increasing latitude. A link between vitamin D (synthesized in the skin by ultraviolet radiation) and decreased risk of MS has epidemiologic support.

**Objective:** To test the hypothesis that higher levels of serum 25-hydroxyvitamin D (25(OH)D) are associated with lower relapse rates in patients with relapsing-remitting MS (RRMS). The biologically active form of vitamin D is 1,25 dihydroxyvitamin D, but the major circulating form is 25(OH)D.

**Design:** Prospective longitudinal cohort study.

**Participants:** The study involved 145 patients with RRMS residing in Tasmania, off the coast of Australia, with a mean age of 45 years (three fourths were female).

**Methods:** Clinical data were collected twice a year: lifestyle and activity levels, with special attention to time spent outdoors, smoking, specific treatment for MS, use of vitamin D supplements, and Expanded Disability Status Scale (EDSS). Patients kept a weekly diary of symptoms, therapies, and infections. Relapses were defined according to the 2001 McDonald criteria. Patients notified investigators of relapses by telephone, with follow-up by a physician or nurse. The accuracy of telephone reporting of relapses was validated in a subset of patients in year 1 of the study. Patients also wore badges 2 days/week, winter and summer, to quantitate ultraviolet exposure. Serum 25(OH)D levels were measured twice a year by immunoassay. Neither study personnel nor patients knew the results of these determinations.

**Results:** The cohort had an average EDSS of 2.8; 80% were on immunomodulatory therapy. Not unexpectedly, 25(OH)D levels were higher in the summer and in patients who spent more time outdoors. They were not higher in patients who took vitamin D supplements. There was a trend toward decreasing 25(OH)D levels with age, body mass index, and EDSS score. Higher levels of 25(OH)D were associated with lower hazards of relapse, with each 10 nmol/L increase translating into a 9% reduction. There was no evidence of a "threshold" effect. Time to first relapse was longer with higher 25(OH)D as well. The association held after adjustment for age, sex, therapy, smoking, physical activity, pregnancy, infections, EDSS at entry, duration of MS at entry, and after patients with frank vitamin D deficiency were excluded. To exclude "reverse causality," patients were stratified by EDSS of >4.5 or ≤4.5, without a change in the findings.

**Conclusions:** The findings support randomized, controlled trials of vitamin D in RRMS.

**Reviewer's Comments:** It might be difficult to convince RRMS patients to enter a randomized clinical trial of vitamin D with a placebo arm. (Reviewer-James W. Schmidley, MD.)
In this study, in childhood-onset epilepsy after long-term follow-up, remote symptomatic epilepsy was associated with the greatest risk of intractability and mortality.

**Objective:** To evaluate the clinical course and outcome in childhood-onset epilepsy with a long duration of follow-up of approximately 15 years. Age at onset of epilepsy ranged from 1 month to 16 years.

**Participants:** The initial cohort with new-onset epilepsy included 494 children. During the follow-up period, 18 children died and 63 were either lost to follow-up or did not respond to the follow-up questionnaire, resulting in 413 who completed follow-up.

**Methods:** Children with new-onset epilepsy were consecutively recruited in a multicenter, hospital-based study in the Netherlands from 1988 to 1992. Subjects were required to have at least 2 unprovoked seizures or 1 episode of unprovoked status epilepticus prior to enrollment.

**Results/Conclusions:** Mean age at seizure onset was 5.5 years. Mean duration of follow-up was approximately 15 years (range, 11 to 17 years). Seizure freedom for >5 years at the end of follow-up had been achieved in 70.9% of the cohort. Mean duration of active epilepsy was 6 years but ranged from 0 to 21 years and strongly correlated with etiology and epilepsy type. Antiepileptic drugs (AEDs) were used in 86%, with a mean duration of therapy of 7.4 years. Seizure freedom was achieved during the first 5 years of follow-up in 35% of subjects. At the time of last follow-up, about one third were still on AED therapy, and 9% had intractable epilepsy with regular seizure recurrence during the last year of follow-up. Idiopathic epilepsy was associated with a greater chance of early control, early remission, and remission overall. Symptomatic epilepsy was associated with a greater risk of relapse and intractability. Risk factors determined in multivariate analysis to predict intractability during the last year of follow-up were non-idiopathic etiology, febrile seizures, no 3-month remission during the first 6 months of follow-up, and early intractability during the first 5 years of follow-up. Of 18 patients who died, 17 had remote symptomatic etiology. Overall, the crude mortality rate for children with epilepsy was about 10 times higher than that of the general population of similarly aged children but was primarily increased in those with remote symptomatic epilepsy, with many deaths related to the underlying condition. Only 2 deaths were thought to be seizure-related.

**Reviewer's Comments:** In this study of children with new-onset seizures who were followed for about 15 years, the outcome was good, with about 70% achieving complete remission or seizure freedom. At the end of the follow-up period, about one third of the cohort was still on AED therapy. Remote symptomatic epilepsy was associated with the greatest risk of intractability and mortality. (Reviewer-Gregory B. Sharp, MD).

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Keywords: Childhood-Onset Epilepsy, Long-Term Outcome

Print Tag: Refer to original journal article
Are Epileptiform Abnormalities Common on EEGs in Healthy Children?

Prevalence of Epileptiform Discharges in Healthy Children—New Data From a Prospective Study Using Digital EEG.

Borusiak P, Zilbauer M, Jenke ACW:

Epilepsia 2010; 51 (July): 1185-1188

In this study, epileptiform electroencephalogram abnormalities were seen in >5% of what was considered to be a cohort of healthy children.

Background: In the past, several studies that evaluated the presence of epileptiform abnormalities on electroencephalogram (EEG) recordings in healthy children utilized analogue recordings on paper. Digitally recorded EEG (DEEG) provides many advantages, including the ability for the interpreter to change sensitivity, filters, montage, and other settings, which should increase the accuracy of interpretation. Several recent reports have suggested an increased prevalence of epileptiform discharges on DEEG in children with behavioral disturbances and attention-deficit/hyperactivity disorder (ADHD).

Objective: To evaluate the frequency of occurrence of epileptiform discharges in healthy children using DEEG, and to compare these results with those from previously published studies using analogue recordings.

Design/Participants: This prospective study was performed at a single center and included 382 healthy children who ranged in age from 6 to 13 years and were admitted for observation following minor head trauma. Approximately 60% were male and 40% female.

Methods: The routine recording was performed for a minimum of 20 minutes and included hyperventilation and photic stimulation. The recordings were analyzed by 2 board-certified clinical neurophysiologists.

Results: Epileptiform discharges were detected in 25 of the 382 children, with an overall prevalence of 6.5%. Localized focal discharges were present on DEEG in 12 children, multifocal discharges were present in 9 children, and generalized or bifrontal spikes were present in 4.

Conclusions: The prevalence of epileptiform abnormalities on DEEG in this group of children is higher than that reported in prior studies using analogue EEG recordings on paper, with a prevalence that ranged from 3.5% to 5%. The frequency of occurrence of epileptiform abnormalities in this group of children is similar to that noted in more recent studies using DEEG to evaluate children with behavioral disturbances, including ADHD.

Reviewer’s Comments: Epileptiform abnormalities are sometimes seen on DEEG recordings performed on healthy children who do not have epilepsy, with a prevalence of just over 6% in this study. This finding would appear to indicate that there may not be a significant relationship between epileptiform abnormalities on DEEG and behavioral disturbances in children. It is important to note that achieving sleep in the DEEG was apparently not a focus of this study. Sleep was achieved during the DEEG in <20% of the recordings in this study. It is possible that the prevalence of epileptiform abnormalities would be increased if sleep was uniformly achieved in the majority of recordings. A prospective study performing DEEG recordings on a population of healthy children selected at random and using techniques such as sleep deprivation to increase the likelihood of sleep during the recording would likely produce more accurate results. (Reviewer-Gregory B. Sharp, MD).

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Keywords: Epileptiform Abnormalities, Digital EEG, Healthy Children

Print Tag: Refer to original journal article
Intravenous levetiracetam can be used as therapy for acute seizures in children and appears to be very safe.

**Background:** Intravenous levetiracetam (IV-LEV) is approved by the Food and Drug Administration for use in patients >16 years of age. Numerous small studies and case reports concerning the use of IV-LEV in children have demonstrated safety and efficacy in the treatment of several seizure types. There have not been any large studies evaluating the use of IV-LEV in the management of acute seizures in children.

**Objective:** To evaluate the effectiveness of IV-LEV in the treatment of acute seizures in children.

**Methods:** A retrospective chart review using the pharmacy database at a single tertiary pediatric center during a 2-year period was performed. All patients up to 18 years of age were included if they were treated with IV-LEV within 30 minutes of an acute seizure with a duration of >5 minutes, had repetitive seizures, or were status epilepticus. Seizure type, IV-LEV dose, and other medications were recorded. Outcome was measured by seizure control at 1, 12, 24, 48, and 72 hours following IV-LEV administration.

**Results:** A group of 73 children was identified who were treated with IV-LEV for acute seizures. Their mean age was 5 years, and the youngest patient age was 1 day. The mean IV-LEV dose was essentially 30 mg/kg with a range of 7 to 90 mg/kg. Three-fourths of the patients were on chronic antiepileptic drug (AED) therapy, and two-thirds received additional abortive therapies in response to the acute seizure. One-third received IV-LEV only. Treatment was for repetitive seizures in approximately 80% of cases, single seizures in 12%, and status epilepticus in 8%. Almost 90% of patients remained seizure free at 1 hour, and the rate decreased at each time point thereafter. Patients treated for single seizures were most likely to remain seizure free at 72 hours. Just over 50% of the patients did well and were discharged from the hospital within 3 days. Logistic regression analysis demonstrated that only the number of AEDs used at baseline predicted response to IV-LEV. A greater number of AEDs used at baseline predicted a less likely response to IV-LEV. Just over 70% of patients were continued on scheduled LEV following the IV loading dose. Change in mood was the most frequently reported adverse effect.

**Conclusions:** IV-LEV was most effective for the treatment of acute seizures in children who were not on multiple AED therapy. A dose of 20 to 40 mg/kg of IV-LEV was typically used, and no major side effects were observed.

**Reviewer's Comments:** IV-LEV can be considered for the treatment of acute seizures and status epilepticus in children of all ages. IV-LEV produces far fewer adverse effects than other abortive seizure medications. It can be appropriately given as monotherapy or in combination with other AEDs. (Reviewer-Gregory B. Sharp, MD).

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Keywords: IV Levetiracetam, Acute Seizures, Children

Print Tag: Refer to original journal article
A high-dose regimen of intravenous levetiracetam can be considered for treating children with very refractory acute repetitive seizures.

**Background:** Treatment of acute repetitive seizures in children can be extremely difficult. Levetiracetam (LEV) has been proven to be effective in the treatment of partial and generalized seizures in children, has minimal adverse effects, and can be tolerated at relatively high dosages. The actual upper limit in dosing has not been defined in children or adults. Absorption after oral administration is rapid and complete, pharmacokinetics is linear, and plasma protein binding is minimal. Elimination is primarily renal, and there is no significant impact on hepatic metabolism of other antiepileptic drugs (AEDs) or other drugs. Rapid infusion of intravenous-LEV (IV-LEV) is safe and well tolerated. It is not excessively sedating, and has little impact on cardiac rhythm, blood pressure, or respiration.

**Objective:** To review the experience of using high-dose IV-LEV for acute seizure exacerbations in children with medically intractable epilepsy.

**Participants:** All 9 children (2 boys, 7 girls) had exacerbations of acute repetitive seizures that occurred during therapy with other AEDs. Admission was in response to frequent repetitive seizures in 8 and occurred during hospitalization in 1 patient. All were having multiple seizures per day, 3 were having multiple seizures per hour, and 1 child had refractory status epilepticus. These children were quite young, ranging from 3 months to 3.5 years of age. All but 1 had symptomatic-related epilepsy. They were on a mean of 3.5 other AEDs. Two were also on oral LEV at a lower dose.

**Methods:** IV-LEV was started at 30 mg/kg every 8 hours on day 1 (90 mg/kg per day). The dose of 30 mg/kg was maintained, and dosing was changed to every 6 hours on day 2 (120 mg/kg per day) and to every 4 hours on day 3 (180 mg/kg per day). On day 4, if seizures persisted and the dose was tolerated, dosing was continued every 4 hours and the individual dose was increased accordingly. Response to therapy and tolerability were assessed with continuous video–electroencephalography and cardiorespiratory monitoring.

**Results:** The IV-LEV dose ranged from 150 to 286 mg/kg per day, with a mean of 228 mg/kg per day. IV-LEV therapy was effective with resolution of acute repetitive seizures in 8 of the 9 children. Seizure frequency was reduced to below baseline in 7 children. Seizure freedom was achieved in 2, an 80% reduction was achieved in 4, and a 50% reduction in seizure frequency was achieved in 1 child. The one child who did not improve experienced an increase in seizures. IV-LEV was otherwise well tolerated in all children without complications. The maximum IV dose was converted to an oral dose and continued at the time of discharge.

**Reviewer’s Comments:** This is an unusual but intriguing treatment protocol that provides another treatment option for consideration in children with acute exacerbations of refractory repetitive seizures. (Reviewer-Gregory B. Sharp, MD).

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**Keywords:** Intractable Epilepsy, Children, Levetiracetam, Acute Seizure Exacerbation

**Print Tag:** Refer to original journal article
CAG Repeats on Abnormal Huntingtin Allele May Cause Late-Onset HD

Late-Onset Huntington Disease With Intermediate CAG Repeats: True or False?

Groen JL, de Bie RMA, et al:

J Neurol Neurosurg Psychiatry 2010; 81 (February): 228-230

Late-onset Huntington disease can be caused by an intermediate number of CAG repeats on the abnormal huntingtin allele.

**Background:** Huntington disease (HD) is caused by an autosomal dominant mutation, consisting of an increase in the number of CAG trinucleotide repeats in the coding region of the huntingtin gene on chromosome 4. The normal allele contains 6 to 26 CAG repeats, and HD results when there are ≥36 repeats on the abnormal one. An allele with 27 to 35 repeats, an "intermediate" number, is not associated with HD, but it is unstable and may expand to pathogenic length when passed from father to child.

**Objective:** To show that a huntingtin allele with an intermediate number of CAG repeats can cause late-onset HD.

**Design:** 2 case reports.

**Results:** One patient was 68 years old when chorea, abnormal behavior, and memory loss began. His sister had a movement disorder and her children had an identical illness, which was genetically proven to be HD (43 CAG repeats on the abnormal allele). The patient's own test for HD showed 31 CAG repeats on 1 allele and 18 on the other. The other patient was 65 years old when dysarthria, chorea, and apathy began. Her sister had a psychiatric disease and jerky movements in her arms. The patient's HD test showed 30 CAG repeats on 1 allele and 17 on the other. Both patients' conditions worsened progressively. Genetic tests for HD like-2, dentatorubropallidoluysian atrophy and spinocerebellar ataxia 3, 14, and 17, were normal. There was no history of use of antipsychotic medications. Laboratory tests for hyperthyroidism, syphilis, Lyme disease, neuroferritinopathy, Wilson's disease, neuroacanthocytosis, Hallervorden-Spatz disease, and systemic lupus erythematosus were negative. The authors diagnosed both patients with HD because of the family history and lack of other diagnosis.

**Conclusions:** Late-onset HD can be caused by an intermediate number of CAG repeats on the abnormal huntingtin allele.

**Reviewer's Comments:** The late onset is in keeping with the known inverse relationship, in HD, between age of onset and number of CAG repeats in the abnormal huntingtin allele. (Reviewer-Marc D. Winkelman, MD).

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Keywords: Huntington Disease, Chorea, Late-Onset Chorea, CAG Repeats

Print Tag: Refer to original journal article
Treatment-induced diabetic neuropathy is a reversible, small-fiber polyneuropathy that follows rapid, sustained regulation of chronic, extreme hyperglycemia.

**Background:** Since the 1930s, case reports have appeared of diabetic patients who develop an acute painful polyneuropathy when their longstanding hyperglycemia has come under control (insulin neuritis).

**Objective:** To provide clinical, physiologic, histologic, and long-term follow-up data on a large cohort of diabetic patients with insulin neuritis, which the authors rename “treatment-induced neuropathy.”

**Design:** Prospective follow-up study at a referral center for diabetic neuropathy.

**Participants:** 16 patients who developed an acute, painful polyneuropathy after rapid and sustained control of chronic, severe hyperglycemia.

**Methods:** All patients were followed for at least 18 months, with serial neurologic examination, semiquantitative assessment of pain and autonomic symptoms, and autonomic function tests. Eight patients had skin biopsies for intraepidermal nerve fiber density (IENFD) in the acute phase of the illness, and 3 had a second biopsy later.

**Results:** 9 patients had type 1 diabetes, and 7 had type 2. Pretreatment glycosylated hemoglobin values ranged from 12% to 17%. Some patients took insulin and some took oral hypoglycemic agents. Pain began 6 to 8 weeks after controlling blood sugar. The pain was severe and responded poorly to treatment with antidepressant, anticonvulsant, and narcotic medications. The location of the pain was stocking-glove in 13 patients and throughout the body in 3. Twelve patients (75%) had orthostatic intolerance. On examination, all patients had impaired sensation of pain and temperature in the distal lower limbs, and >50% had hyperalgesia and allodynia. None had muscle weakness. Tendon reflexes and other sensory modalities were not reported. Seven patients (44%) had diabetic retinopathy. Test results of cardiovascular sympathetic and parasympathetic function were abnormal in 11 patients (69%). Initial skin biopsies showed reduced IENFD in all patients. Over the course of the study, pain improved in all patients, by 50%, in 15 months, on average (range, 12 to 18 months). On follow-up evaluation at 18 months, autonomic symptoms and function improved more in patients with type 1 than type 2 diabetes, as did IENFD. Retinopathy worsened; at 18 months, all patients had developed it.

**Conclusions:** Treatment-induced diabetic neuropathy is a reversible, small-fiber polyneuropathy that follows rapid, sustained regulation of chronic, extreme hyperglycemia. The neuropathy occurs in parallel with worsening diabetic retinopathy, suggesting a common pathophysiologic mechanism.

**Reviewer’s Comments:** Diabetic neuropathic cachexia, another small-fiber polyneuropathy that develops early in the course of diabetes, differs from treatment-induced diabetic neuropathy in 2 ways: patients have lost much weight and their blood sugar is very high when symptoms begin. (Reviewer-Marc D. Winkelman, MD.)

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Keywords: Insulin Neuritis, Tx-Induced Diabetic Neuropathy, Painful Polyneuropathy, Autonomic Neuropathy

Print Tag: Refer to original journal article
Mexiletine is effective in reducing myotonia in myotonic dystrophy type 1 patients and is safe in those without cardiac disease.

**Background:** Myotonia is a frequently disabling symptom in patients with myotonic dystrophy (DM1). Usual treatments, based mostly on uncontrolled series, are sodium channel blockers (phenytoin, carbamazepine, and mexiletine), calcium channel blockers, quinine, and benzodiazepines. Mexiletine has been advocated based on 1 randomized and single-blinded study of patients with heterogeneous causes of myotonia including DM1.

**Objective:** To determine if mexiletine is safe and effective in treating myotonia in DM1.

**Design:** 2 randomized, double-blind, placebo-controlled crossover trials in 1 academic medical center.

**Participants:** Adult patients with DM1 and confirmed unstable CTG repeat expansion were recruited. Inclusion criteria included enough grip strength to grasp a handle and the ability to walk 15 feet independently. Patients with second- and third-degree heart block, atrial fibrillation/flutter, ventricular arrhythmia, cardiomyopathy, and coronary artery disease were excluded.

**Methods:** Patients randomized in the first trial received 150 mg 3 times daily (TID) of mexiletine versus placebo, while they received 200 mg TID versus placebo in the second trial. The patients were treated for two 7-week periods separated by a 4-week washout period. Grip myotonia was measured by an automated computer program as relaxation times (RT) after a 3-second maximal voluntary isometric contraction. The primary outcome was the average RT time to decline in peak force (PF) from 90% to 5%. Secondary outcomes included the average RTs from 90% to 10% and 50% to 5% and the average PFs. Electrocardiograms were obtained at baseline and at frequent intervals during the study.

**Results:** 20 patients participated in each trial. The median CTG repeats were 500 in both trials. There was an equal and significant reduction in RT with mexiletine versus placebo in the 150 mg TID trial (1.32 seconds vs 2.55 seconds; treatment effect, -1.23; mean reduction, 48%; \( P =0.0004 \)) and the 200 mg TID trial (1.27 seconds vs 2.63 seconds; treatment effect, -1.36; mean reduction, 52%; \( P =0.001 \)). In both trials, 17/18 (94%) had a shorter RT on mexiletine compared to placebo. Similar reductions were seen in the 90% to 10% and 50% to 5% RT in mexiletine-treated groups versus placebo. PF improved in the 150 mg TID group only (\( P =0.04 \)). Mexiletine was well tolerated with only mild gastrointestinal disturbances. One patient on 200 mg TID dropped out due to diarrhea. There were no significant changes in electrocardiograms between groups.

**Conclusions:** Short-term treatment with mexiletine is safe and effective in reducing myotonia in DM1.

**Reviewer's Comments:** This study confirms that short-term use of mexiletine is safe and effective in reducing myotonia in DM1 patients with no cardiac disease. It is still not clear whether mexiletine is also safe in patients with DM1 with heart disease. As suggested by the authors, these patients should undergo cardiac consultations before treatment with mexiletine is initiated. (Reviewer-Bashar Katirji, MD).

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**Keywords:** Myotonic Dystrophy Type 1, Treatment, Mexiletine, Dosage, Cardiac Dz

Print Tag: Refer to original journal article
How to Distinguish A-CIDP From GBS-TRF

Distinguishing Acute-Onset CIDP From Fluctuating Guillain-Barré Syndrome: A Prospective Study.
L Ruts, J Drenthen, et al:
Neurology 2010; 74 (May 25): 1680-1686

Background: Guillain-Barré syndrome (GBS) is a monophasic illness and reaches its nadir by 4 weeks, while chronic inflammatory demyelinating polyneuropathy (CIDP) is a progressive or relapsing-remitting disease and progresses over >2 months. When treated with plasma exchange or IV immunoglobulin (IVIg), GBS may show treatment-related fluctuations (GBS-TRF) in up to 16% of patients. On the other hand, acute-onset CIDP (A-CIDP) may reach nadir in 8 weeks, and a chronic course is reported in approximately 15% of patients. It is important to distinguish GBS-TRF from A-CIDP since they have different therapies and prognosis.

Objective: To provide criteria that may help to distinguish GBS-TRF from A-CIDP.

Methods: Patients with GBS were collected prospectively from 55 Dutch medical centers between 2005 and 2008 and followed for 1 year. Among 164 GBS patients seen, 24 had fluctuating course and were included in this study. All were followed clinically using the GBS disability score (0 to 6 scale) and the Medical Research Council (MRC) sumscore (from 0 "paralysis" to 60 "normal strength"). A GBS-TRF or A-CIDP exacerbation was defined as a worsening GBS score of at least 1 grade or a decrease in MRC sumscore by >5 points after similar improvement or stabilization for >1 week. The numbers of exacerbation in A-CIDP were only counted before maintenance therapy with IVIg or steroids was started.

Results: Among the 164 patients selected, 16 (10%) had GBS-TRF and 8 (5%) had A-CIDP. One-third of the GBS patients had a second TRF, but none had >2 TRFs. In contrast, one-half (4 of 8) of the A-CIDP patients had >2 exacerbations ($P = 0.01$). There was a significant difference in the median number of days to reach nadir of first TRF/exacerbation from onset of disease between the GBS-TRF and A-CIDP patients (18 vs 51 days [$P = 0.00$], with nonoverlapping ranges of 15 to 27 days vs 31 to 63 days, respectively). The second TRF/exacerbation also differed significantly between GBS-TRF and A-CIDP patients (median, 38 days vs 105 days; $P = 0.01$). Electrophysiological signs of demyelination were much more common in A-CIDP than GBS-TRF.

Conclusions: A-CIDP should be considered when GBS patients deteriorate after 8 weeks or have >2 TRF. Patients with GBS-TRF have more cranial nerve involvement and electrophysiological signs of demyelination.

Reviewer's Comments: Despite the small number of patients, this is a very useful study that should help clinicians deciding whether to commit a patient to chronic maintenance therapy or not. However, despite reading this manuscript several times, I could not decipher how the authors separated their patients into the GBS-TRF versus A-CIDP before they initiated their statistical analysis. (Reviewer-Bashar Katirji, MD).

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Keywords: Guillain-Barré Syndrome, Chronic Inflammatory Demyelinating Polyneuropathy

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