AANEM Case Report # 4
Guillain-Barré Syndrome

David H. Weinberg, MD
ABSTRACT: A 57-year-old woman developed rapidly progressive, symmetric, extremity weakness, facial diplegia, ophthalmoplegia, respiratory insufficiency, and sensory ataxia over a 3-week period. Electrodiagnostic studies were performed on days 6, 13, and 50 following the onset of weakness. Motor nerve conduction abnormalities were the predominant findings. Prolonged motor distal latencies, prolonged or absent F waves, and partial motor conduction blocks were present and form the diagnostic features of an acquired, demyelinating polyneuropathy. Abnormalities in sensory nerve conductions and blink reflexes were also present. Guillain–Barré syndrome was diagnosed prompting the initiation of therapeutic plasma exchange. The patient’s clinical status continued to worsen over the next 10 days before stabilizing. Considerable improvement in extremity strength, ocular motility, and respiratory function occurred in the subsequent weeks. Well-planned and well-executed electrodiagnostic studies generate key adjunctive data to the clinical diagnosis of Guillain–Barré syndrome.

© 1999 American Association of Electrodiagnostic Medicine.


AAEM CASE REPORT 4:
GUILLAIN–BARRÉ SYNDROME

DAVID H. WEINBERG, MD

Department of Neurology, Tufts University School of Medicine, St. Elizabeth’s Medical Center, Boston, Massachusetts 02135-2907, USA

Accepted 16 July 1998

Guillain–Barré syndrome is a clinically defined disorder of rapidly progressive weakness and aberrant sensation. It represents the most important acute polyneuropathy (PN) in clinical practice and, since the advent of successful therapy, one of the most gratifying to manage. Electrodiagnostic studies are not considered essential to make the diagnosis in the typical case; however, the integration of these data is often crucial in the rapid diagnostic process that is necessary to initiate early therapy.

CASE REPORT

History. A 57-year-old woman was well until 7 days prior to admission when she developed severe low-back pain. Two days later, she noted a “tingling” sensation bilaterally in the toes and feet and a “buckling” feeling in both knees when walking up or down stairs. Over the 2 days prior to admission, the paresthesias became prominent in the feet and extended to the fingers and hands. The difficulty walking became severe and she needed to crawl on stairs. Additionally, she noted hand clumsiness and weakness, slurring of speech, and “doubling” of her vision. The midback pain remained severe.

She had received a flu shot about 3 weeks prior to the onset of symptoms. She denied fever, headache, shortness of breath, dizziness, neck pain, or stiffness, bowel or bladder changes, similar prior symptoms, recent family illness, or family history of episodic weakness.

Her only past medical history was type II diabetes mellitus treated with glipizide (Glucotrol®).

Examination. The blood pressure was 180/70 with a regular heart rate of 70–90 bpm, comfortable respirations at 16/min, and a temperature of 99°F. Cranial nerve abnormalities included right eye adductor weakness with horizontal image separation during left gaze on red glass testing and severe, bilateral, peripheral facial paresis with a lingual dysarthria.

Abbreviations: AAN, American Academy of Neurology; CIDP, chronic inflammatory demyelinating polyneuropathy; CMAP, compound motor action potential; CSF, cerebrospinal fluid; CV, conduction velocity; DL, distal latency; DTR, deep tendon reflex; EMG, electromyography; FVC, forced vital capacity; GBS, Guillain–Barré syndrome; Ig, immunoglobulin; IVIg, intravenous gammaglobulin; MGUS, monoclonal gammopathy of undetermined significance; MRC, Medical Research Council; NCS, nerve conduction studies; NIF, negative inspiratory force; PN, polyneuropathy; SNAP, sensory nerve action potential

Key words: Guillain–Barré syndrome; demyelinating polyneuropathy; nerve conduction studies; electromyography

Correspondence to: American Association of Electrodiagnostic Medicine, 421 First Avenue S.W., Suite 300 East, Rochester, MN 55902, USA

CCC 0148-639X/99/020271-11
© 1999 American Association of Electrodiagnostic Medicine. Published by John Wiley & Sons, Inc.
Motor examination revealed generalized limb weakness in the 4–4+/5 range except for 3/5 weakness of the gluteals and sparing of the deltoids, biceps, and quadriceps [Medical Research Council (MRC) scale]. Myotatic reflexes were characterized by absent ankle, knee, and right triceps reflexes; 1/4 left triceps reflex; and 2/4 bilateral biceps and brachioradialis reflexes. Plantar responses were flexor bilaterally. Sensory examination revealed decreased pin, light touch, and temperature sensitivity in a circumferential and graded pattern over the feet to the midsacral level as well as over the hands to the distal forearms, with a band of hyperesthesia over approximately the T8 dermatome bilaterally without the suggestion of a sensory level.

Bedside forced vital capacity (FVC) on admission was 2 L while the negative inspiratory force (NIF) was −60 cm H2O.

**Laboratory Tests.** Lumbar puncture produced clear, colorless fluid with a cerebrospinal fluid (CSF) protein of 168 mg%, (normal 15–45 mg%), glucose of 146 mg/dL (serum 206 mg/dL), and cell counts of 3 red blood cells/mm³ and 2 white blood cells/mm³. The serum immunofixation detected an elevated immunoglobulin (Ig)M at 365 mg/dL (normal 60–263 mg/dL) with an IgM lambda type monoclonal spike. Stool *Campylobacter jejuni* antigen and routine viral titers were negative. Erythrocyte sedimentation rate and angiotensin-converting enzyme values were normal.

**CLINICAL COURSE**

In the first 2 days of hospitalization, the patient developed oblique diplopia with evident superior rectus weakness. Plasma exchange was initiated the morning after admission and six 2.5-L exchanges (0.25 L/kg) were completed over the next 9 days. On day 3, she became mildly tachycardic while maintaining a stable blood pressure. The FVC decreased to 1.5 L with a NIF of −44 cm H2O. Facial diplegia developed with moderately severe proprioceptive loss in both feet. Proximal leg weakness became considerably worse with loss of antigravity strength in the iliopsoas and all gluteal muscles. The diplopia continued to worsen and by day 5, all ductions were abnormal. Over the next 5 days, there were increased paresthesias in both hands and worsened proprioceptive function in both legs including impaired vibration at both hips. On day 10, the FVC increased to 2.4 L with a NIF of −60 cm H2O. Transfer to the rehabilitation service occurred 12 days after admission. The upper-extremity strength at that time was near normal proximally with modest intrinsic hand muscle and finger extensor weakness. There was persistent proximal leg and pelvic weakness but distal muscles were near normal. Deep tendon reflexes (DTRs) were still absent except for the left-biceps jerk rated at +1. Vibration was absent below the knees and still abnormal at the level of the hips and hands. Examination on day 50 was much improved but the patient still required a walker for safe ambulation due to the proprioceptive disturbance.

**ELECTRODIAGNOSTIC EXAMINATION**

**Methods.** All nerve conduction studies (NCSs) were performed with standard percutaneous stimulation and surface recordings techniques. A number of different proximal and distal stimulation locations were used in obtaining the compound motor action potentials (CMAPs). Recorded variables are listed in the Tables 1 and 2, as are normal values. F waves were obtained at the distal motor stimulation point and the minimal latency of 20 consecutive stimulations was recorded. Sensory nerve action potentials (SNAPs) were performed orthodromically. All amplitudes were measured baseline to negative peak. Electrical stimulation for the blink reflexes was performed over each supraorbital notch with simultaneous recording from bilateral orbicularis oculi muscles.

Needle examination was conducted with disposable concentric needle electrodes. Spontaneous activity was judged on the conventional 0–4 graded scale with 0 = normal and +4 = continuous fibrillations and/or positive sharp waves. A similar subjective 0–4 scale was applied to the motor unit potential characteristics of amplitude, duration, configuration (phases), and recruitment, although individual units were inspected and measured on the trigger scope.

**Nerve Conduction Studies.** Three studies were performed during the course of the illness on days 6, 13, and 50 following the development of weakness. Key left-sided sequential results are summarized in Tables 1 and 2. Blink reflexes were absent bilaterally in the first study but present on the left side 7 days later (Fig. 1). The left-sided stimulation ipsilateral R1 and R2 potentials (left-sided responses) and right-sided stimulation contralateral R2 potential (left-sided response) all had markedly prolonged latencies. No responses could be obtained on the right side following stimulation on either side. These findings most likely represent conduction slowing in the left-facial nerve and conduction block in the right-facial nerve.

The first study was characterized by reductions in
some motor amplitudes, a modest prolongation in some distal motor latencies, absent peroneal and tibial F waves, and a single partial motor conduction block (in the peroneal nerve below the fibular head). The median and ulnar sensory amplitudes were also reduced.

One week later, there was a new tibial nerve amplitude decrement (proximal to distal) suggestive of a partial conduction block, further overall reductions in the motor amplitudes, and a significant prolongation of many motor distal latencies (DLs) with stable conduction velocities (CVs). The median SNAP was now absent and although the sural amplitude was unchanged, the DL was prolonged. Further insight into the underlying process is gained by examining the individual CMAP waveforms, especially the late components (Fig. 2). By rastering and superimposing a number of tracings at a reduced sensitivity (i.e., 50–500 µV), even low-amplitude time locked or periodically blocked components are easily identified. The dramatic prolongation of the tibial CMAP duration in Figure 2 reflects demyelination in distal segments with resultant desynchronization of the motor volleys.

In the final study, the distal motor amplitudes were improved but nearly all the motor DLs were prolonged and the F waves and SNAPs were either absent or prolonged.

**Needle Electromyography.** The initial needle electromyography (EMG) study was characterized by normal spontaneous activity, motor unit configuration, and normal compound muscle action potentials (CMAPs) with no evidence of insertional activity or neurogenic changes. The needle EMG findings were consistent with a questionablePostsynaptic Depression (PSD) at the neuromuscular junction, which is a common finding in some cases of Guillain–Barré Syndrome (GBS).

### Table 1. Summary of three sequential motor nerve conduction studies (left side only).

<table>
<thead>
<tr>
<th>Test #</th>
<th>Nerve</th>
<th>Amplitude (mV)</th>
<th>Latency (ms)</th>
<th>Conduction velocity (ms)</th>
<th>Duration* (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>6.0</td>
<td>ND</td>
<td>6.3</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>5.9</td>
<td>4.6</td>
<td>6.6</td>
<td>&gt;4.4</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>6.0</td>
<td>4.1</td>
<td>6.5</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>6.0</td>
<td>4.1</td>
<td>5.6</td>
<td>12.7</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>F wave</td>
<td>30.7</td>
<td>35.5</td>
<td>36.4</td>
</tr>
</tbody>
</table>

**Table 2. Summary of three sequential sensory nerve conduction studies (left side only).**

<table>
<thead>
<tr>
<th>Test #</th>
<th>Nerve*</th>
<th>Amplitude (µV)</th>
<th>Peak latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (wrist)</td>
<td>4.4</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Ulnar (wrist)</td>
<td>9.1</td>
<td>9.2</td>
</tr>
<tr>
<td></td>
<td>Sural (calf)</td>
<td>10.6</td>
<td>14.0</td>
</tr>
</tbody>
</table>

**Table 3. Summary of three sequential sensory nerve conduction studies (left side only).**

<table>
<thead>
<tr>
<th>Test #</th>
<th>Nerve</th>
<th>Amplitude (µV)</th>
<th>Peak latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (wrist)</td>
<td>4.4</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Ulnar (wrist)</td>
<td>9.1</td>
<td>9.2</td>
</tr>
<tr>
<td></td>
<td>Sural (calf)</td>
<td>10.6</td>
<td>14.0</td>
</tr>
</tbody>
</table>

*Negative peak, normal <15% distal to proximal.

**Table 4. Summary of three sequential sensory nerve conduction studies (left side only).**

<table>
<thead>
<tr>
<th>Test #</th>
<th>Nerve</th>
<th>Amplitude (µV)</th>
<th>Peak latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (wrist)</td>
<td>4.4</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>Ulnar (wrist)</td>
<td>9.1</td>
<td>9.2</td>
</tr>
<tr>
<td></td>
<td>Sural (calf)</td>
<td>10.6</td>
<td>14.0</td>
</tr>
</tbody>
</table>

*Negative peak, normal <15% distal to proximal.

AAEM Case Report: GBS MUSCLE & NERVE February 1999 273
FIGURE 1. Left blink reflex. Electrical stimulation was performed over the left supraorbital notch. The upper tracing was recorded from the ipsilateral orbicularis oculi muscle and the lower tracing from the same muscle on the right. The ipsilateral R1 (open arrow) and R2 (solid arrow) responses are markedly prolonged (upper limits of normal = 13 ms R1, 41 ms ipsilateral R2) while the contralateral R2 is absent.

FIGURE 2. Tibial CMAP. Recorded utilizing a split screen F-wave program to visualize the late components. Five trials are superimposed. No F waves are present. Sweep speed: (A) 5 ms/div; (B) 10 ms/div. Sensitivity: left of vertical bar, 50 µV/div; right of vertical bar, 200 µV/div for each.
tion, and motor unit activation but with reduced motor unit recruitment in every examined muscle including the mentalis. The second study, 1 week later, was similar except for further reductions in the recruitment pattern of proximal muscles. A small number of fibrillation potentials and positive sharp waves were present in multiple distal muscles 1 month later with a modest improvement in the recruitment pattern and continued stable motor unit configurations.

**Interpretation.** All three studies are markedly abnormal. The first has multiple features suggestive of an acquired demyelinating polyneuropathy but they became more prominent with each study. In the final examination, almost all the motor DLs are prolonged and the sensory potentials and F waves are either absent or prolonged. In all three studies combined, only two CVs were slowed into the “demyelinating range” (Table 3).1,19 These findings are characteristic of the Guillain–Barré syndrome.

**DISCUSSION**

Guillain–Barré syndrome (GBS) is an acute, acquired, multifocal demyelinating disease of the peripheral nerve. Many clinical forms of the disease have been described but the typical and “defining” clinical features are demonstrated by this case: acute, symmetric, progressive weakness with distal paresthesias and areflexia. Involvement of facial, oropharyngeal, oculomotor, and respiratory muscles61 is seen as are features of a dysautonomia23,77 and complaints of pain.52,61

Most patients reach their peak clinical deficit in the first 2 weeks of the illness but some will progress for 3–4 weeks. A plateau of days to weeks may follow but once improvement is seen, acute relapses in untreated patients are uncommon.

Plasma exchange became the standard of care for significantly disabled, recent-onset GBS patients in the mid-1980s with the publication of two large randomized trials.28,66 The optimal volume and number of exchanges is uncertain but the typical regimen of five 50-mL/kg exchanges may not be necessary and four 40-mL/kg exchanges may have equivalent benefit.29 Recently, intravenous gammaglobulin (IVIg) infusions have been demonstrated to have similar efficacy to plasma exchange13,56,69,73 and have been embraced in clinical practice due to ease of administration and safety. The combination of plasma exchange followed by IVIg infusions conferred no extra benefit compared with either therapy alone.56 Unfortunately, posttreatment relapses have been documented for both treatments.18,59 The role of high-dose intravenous steroids is currently unsettled and the general consensus recommendation is that it not be used at this time.24,34,37,40

The differential diagnosis of suspected GBS cases is diverse and depends on the nature of the clinical presentation. Some of the most important conditions include acute myelopathies, vasculitic neuropathies, critical illness polyneuropathy, mononeuritis multiplex, Lyme disease, tick paralysis, periodic paralysis, acute intoxications (especially arsenic or organophosphates, among many others), myasthenia gravis, botulism, poliomyelitis, acute intermittent porphyria, neoplastic meningitis, and fulminant myositis.58 Most are easily excluded by the clinical examination or simple ancillary testing but in some situations others can be quite difficult to eliminate. An evolving acute myelopathy misdiagnosed as GBS is the most common early diagnostic error seen in the author’s referral patients.

The immunopathogenesis of GBS is well established but the details remain controversial. The cell-mediated demyelination of peripheral nerves has been documented in experimental allergic neuritis38 (the only animal model for GBS) and perivenular T-cell infiltrates have been noted in the nerves of GBS patients.5,39 Several lines of evidence in recent years have also implicated the humoral immune system but their primary role in disease induction is still questioned. Direct antibody damage or antibody-targeted, macrophage-mediated destruction of my-

**Table 3. Electrodiagnostic criteria for a chronic demyelinating polyneuropathy.**

<table>
<thead>
<tr>
<th>Must meet three of the following four criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Δ CV in ≥2 nerves</td>
</tr>
<tr>
<td>a. &lt;80% LLN if ampl &gt;80% of LLN</td>
</tr>
<tr>
<td>b. &lt;70% LLN if ampl &lt;80% of LLN</td>
</tr>
<tr>
<td>2. Partial CB or Abn TD in ≥1 motor nerves (not over compression sites)</td>
</tr>
<tr>
<td>a. Partial CB: &lt;15% Δ in duration + &gt;20% ↓ −p area or p-p ampl (proximal to distal sites)</td>
</tr>
<tr>
<td>b. Partial CB or Abn TD: &gt;15% Δ in duration + &gt;20% ↓ −p area or p-p ampl (proximal to distal sites)</td>
</tr>
<tr>
<td>3. ↑ distal latency in ≥2 nerves</td>
</tr>
<tr>
<td>a. &gt;125% ULN if ampl &gt;80% LLN</td>
</tr>
<tr>
<td>b. &gt;150% ULN if ampl &lt;80% LLN</td>
</tr>
<tr>
<td>4. Absent F waves or ↑ minimum latencies in ≥2 nerves</td>
</tr>
<tr>
<td>a. &gt;120% ULN if CMAP ampl &gt;80% LLN</td>
</tr>
<tr>
<td>b. &gt;150% ULN if CMAP ampl &lt;80% LLN</td>
</tr>
</tbody>
</table>

Adapted from Ad Hoc Subcommittee of the American Academy of Neurology AIDS Task Force1 with permission of the authors. ↑, increase; ↓, decrease; CV, conduction velocity; ampl, amplitude; LLN, lower limit of normal; ULN, upper limit of normal; Abn, abnormal; CB, conduction block; TD, temporal dispersion; Δ, change; −p, negative peak; p-p, peak to peak; CMAP, compound muscle action potential.
lin have both been hypothesized as a final effector pathway in at least some patients.\textsuperscript{39} Perhaps the disease is a combination of T-cell- and B-cell-mediated damage functioning in some synergistic manner.\textsuperscript{36}

The trigger for the aberrant autoimmune response in GBS is unknown. Many patients report an antecedent viral illness but no consistent agent is identified. \textit{Campylobacter jejuni} is responsible for many of the diarrheal illnesses that have long been recognized to precede some GBS cases. The patient in this case had a flu shot about 3 weeks prior to the onset of symptoms. The relationship between immunizations and GBS has been debated for many years. The most visible episode was the experience with the 1976 swine-flu vaccine program. Extensive epidemiological investigations were criticized on technical grounds but ultimately it was concluded that exposure to the vaccine carried a small but definable increased risk of developing GBS.\textsuperscript{41} The relationship to other vaccine exposures has been either unconvincing or absent in a number of other studies.\textsuperscript{61} The patient also had a low-titer serum IgM lambda monoclonal gammopathy without evidence of an associated systemic illness. This condition, described as “monoclonal gammopathy of undetermined significance” (MGUS), has been associated with demyelinating polyneuropathies but unlike this case, the course is chronic or subacute, and sensory symptoms predominate.\textsuperscript{33} No GBS case has been attributed to or associated with a MGUS.\textsuperscript{61}

The diagnosis of GBS remains essentially a clinical process. The recognition of the “classic” clinical syndrome is straightforward, even to the inexperienced practitioner. Unfortunately, the early clinical features often contain enough ambiguity to generate diagnostic doubt and potentially delay the initiation of treatment. The first clinical diagnostic paradigm for GBS was generated under the auspices of the National Institute of Neurological and Communicative Disorders and Stroke in 1978 for GBS case ascertainment related to the swine-flu vaccine assessment and it remains a reliable clinical guide.\textsuperscript{6} The core diagnostic requirements are bilateral weakness and areflexia but other thoughtful supportive or exclusionary diagnostic features are included (Table 4). Unfortunately, not all cases fall within either the inclusions or the exclusions, especially early in the course of the illness. For example, the author and colleagues have recently seen patients with preserved myotatic reflexes in weak muscles, pure motor or pure sensory variants, and early bladder involvement, all clinical exclusions in the protocol. Several attempts have been made to improve the sensitivity of clinical protocols while maintaining a high level of specificity.\textsuperscript{2,4,7,48,70} The major purpose of these structured diagnostic tools is the consistent selection of cases for treatment protocols, and the clinician should apply them in only a general way as a review of the major diagnostic features.

Electrodiagnostic studies provide key adjunctive data in the diagnostic process. Unfortunately, the electrophysiological abnormalities are often modest or nonspecific early in the course of the disease—at the time when the greatest diagnostic specificity is desired. It is important to stress that the clinical presentation may have some atypical features when the electrodiagnostic tests are normal or have only nonspecific signs of a polyneuropathy, and the CSF protein is still normal. Treatment at times is initiated before a final diagnostic conclusion is reached. The goal of the initial electrodiagnostic study is to seek definitive signs of an acute demyelinating polyneuropathy or evidence for alternative diagnoses realizing that neither may be present.

Numerous attempts have been made to define the electrodiagnostic characteristics of demyelinating polyneuropathies. The studied variables were chosen to reflect different measures of conduction slowing or conduction block which are the electrophysiological hallmarks of peripheral nerve demyelination. It has long been recognized that axonal

### Table 4. Diagnostic criteria for Guillain–Barré syndrome.

<table>
<thead>
<tr>
<th>Features required for the diagnosis</th>
<th>Features strongly supportive of the diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive weakness in both arms and both legs</td>
<td>Rapid progression of symptoms, up to 4 weeks</td>
</tr>
<tr>
<td>Areflexia</td>
<td>Relative symmetry of signs and symptoms</td>
</tr>
<tr>
<td></td>
<td>Mild sensory symptoms or signs</td>
</tr>
<tr>
<td></td>
<td>Cranial nerve involvement, especially bifacial weakness</td>
</tr>
<tr>
<td></td>
<td>Recovery beginning 2–4 weeks after progression ceases</td>
</tr>
<tr>
<td></td>
<td>Autonomic dysfunction</td>
</tr>
<tr>
<td></td>
<td>Absence of fever at onset of symptoms</td>
</tr>
<tr>
<td></td>
<td>Elevated CSF protein</td>
</tr>
<tr>
<td></td>
<td>CSF mononuclear cell count of 10 or less/mm(^3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features casting doubt on the diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marked, persistent asymmetry of weakness</td>
</tr>
<tr>
<td>Persistent bladder and bowel dysfunction</td>
</tr>
<tr>
<td>Bladder or bowel dysfunction at onset</td>
</tr>
<tr>
<td>Sensory level</td>
</tr>
<tr>
<td>More than 50 mononuclear leukocytes/mm(^3) in CSF</td>
</tr>
<tr>
<td>Presence of polymorphonuclear leukocytes in CSF</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features excluding the diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of toxic neuropathy, porphyria, poliomyelitis, botulism, or hysterical paralysis</td>
</tr>
<tr>
<td>Recent diphtheria</td>
</tr>
<tr>
<td>Pure sensory syndrome</td>
</tr>
</tbody>
</table>

*Adapted from Asbury and colleagues\textsuperscript{6} with permission of the authors. CSF, cerebrospinal fluid.*
nerve damage can increase DLs, slow CVs, and prolong F-wave latencies with loss of the fastest conducting myelinated fibers which determine these measurements. The degree of abnormality has been used to differentiate the small changes that are common in axonal diseases and the larger abnormalities considered characteristic of the “demyelinating range.”

One of the early protocols designed for chronic demyelinating neuropathy required marked slowing of CV and prolongation of DLs in at least two nerves, and conduction block and markedly prolonged F-wave latencies in at least one nerve. Although very specific, these criteria were not sensitive and several modifications followed. The most comprehensive criteria for a demyelinating neuropathy was generated by a working group of the American Academy of Neurology (AAN) for the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). The group defined not only the required types of abnormalities but included standardized procedures for such determination (Table 3). The same four types of nerve conduction abnormalities were utilized as described by Kelly but the AAN group required abnormalities in only three of the four subcategories and refined the definitions to adjust for changes in CMAP amplitude and/or duration. The group also included temporal dispersion as a demyelinating characteristic in the conduction block category.

While these electrophysiological measurements are sensitive for different regions of peripheral nerve demyelination, it has become clear that the distribution of nerve involvement in GBS differs from CIDP. For example, it has been suggested by Brown and Snow that the most common sites of nerve involvement of GBS are sensitive for different regions of peripheral nerve demyelination, it has become clear that the distribution of nerve involvement in GBS differs from CIDP. The group also included temporal dispersion as a demyelinating characteristic in the conduction block category.

For example, it has been suggested by Brown and Snow that the most common sites of nerve involvement in GBS are not randomly distributed throughout the nerve. The distal motor nerve segments were most vulnerable with common involvement in the most proximal nerve segments and in areas prone to compressive mononeuropathies. The reason for this distribution is uncertain but the group’s authors cite the relative deficiency in the blood–nerve barrier in these regions as a potential explanation.

The electrophysiological abnormalities in most major GBS studies also favor the distal and proximal nerve segments with alterations in motor DLs and F-wave latencies being more common than slowed CV or conduction block in the main segments of the commonly studied nerves. Others have proposed that some patients have a more widespread distribution of involvement with sequential areas of demyelination scattered along the course of the motor nerve. The early preservation of motor CVs in most GBS patients would seem to support the former position since numerous demyelinated segments along the course of the nerve should cumulatively slow the CV over the conventional 100–300-mm nerve segments studied. There may well be different electrophysiological subpopulations of GBS patients reflecting varying distributions of demyelinated nerve segments.

Structured electrophysiological protocols serve as research tools for the selection of study patients. The clinical electrophysiological medicine consultant is not restricted to rigid criteria in the evaluation of the prospective GBS patient. The presence of “demyelinating” NCS abnormalities (Table 3) in at least two nerves in regions not typical for compressive mononeuropathies, preferably in both an arm and a leg, or a limb and the face is preferable. Procedures not included in the conventional criteria may be useful to make these judgments as demonstrated in the following examples:

1. Blink reflexes in combination with facial CMAPs are useful in assessing conduction in the commonly involved trigeminal and facial nerves (see below). The yields are highest in patients with facial signs and symptoms. They are particularly useful in patients with a pre-existing or suspected axonal polyneuropathy since the interpretation of limb conductions can be complicated and blink reflexes are rarely abnormal in this setting.

2. The expansion of conventional conduction techniques can clarify the significance of some nonspecific abnormalities. This is best exemplified by the prolongation of the median motor DL with stimulation at the wrist. Stimulation of the median motor nerve in the palm will allow separation of distal median slowing in the terminal fibers from slowing across the carpal tunnel.

3. Motor nerve root stimulation can be used to assess conduction velocities and conduction block in the most proximal nerve segments only indirectly evaluated (by F-wave latencies) in conventional NCSs. Although subject to more technical errors than conventional NCSs, both cervical and lumbar root stimulation can be obtained in most patients. It is most useful when limb weakness is unexplained by conventional distal NCS data.

4. Median and tibial somatosensory evoked potentials can occasionally be helpful in identifying proximal sensory involvement. However, evoked potentials are less sensitive measures than NCS abnormalities and these...
The blink reflexes in the current study demonstrate the utility of the procedure in GBS. In study #1, all potentials were absent bilaterally (both R1 and R2). One week later, the left R1 and left R2 (following stimulation on both sides) were present while all right-sided responses remained absent (following stimulation on both sides) at a time when both facial CMAPs were present. This can best be explained by bilateral, proximal facial nerve conduction blocks on the initial study, and left-sided facial nerve conduction slowing with a persistent right-sided conduction block on the second study. The conduction disturbance must be in the proximal facial nerve because: (1) the afferent trigeminal volley on the left reached the brain stem as evidenced by the left-sided R1 response; (2) the afferent trigeminal volley on the right reached the brain stem as evidenced by the left-sided R2 response; and (3) the facial nerve CMAPs are present bilaterally without distal conduction slowing.

What then are the electrodiagnostic features of early GBS? It is clear that the NCS abnormalities become more prominent during the initial weeks of the disease, even if the patient’s clinical status is improving.2,47 Few studies have systematically examined NCS features in the first week of the disease yet this is precisely the time when therapeutic decisions are made. Proximal conduction abnormalities (manifest as impersistent or absent F waves) were the most common finding in 41 patients studied in the first 6 days of the illness,63 either alone (37%) or in combination with other abnormalities (an additional 39%). Both CV slowing in the demyelinating range and conduction block were uncommon (12% and 2%, respectively). Sensory responses are much less likely to be abnormal during the first study or at any time in the illness, and when abnormal, they are less likely to have demyelinating characteristics.2,47,63,68

The comprehensive study of early electrodiagnostic testing in clinically diagnosed GBS was part of the Dutch Guillain–Barré Study Group project assessing the therapeutic efficacy of IVIg.48 The first EMG was completed a mean of 6 days after the onset of weakness (range 2–15 days). Using their own electrophysiological diagnostic criteria (Table 5), the group reported a sensitivity of 60% for identifying demyelinating PN at the first test which increased to 72% at the third study (mean 34 days). Unfortunately, these diagnostic criteria are not yet adequately tested against other neuropathies and the data published to this point do not detail the individual conduction components to determine which are the most sensitive measures.

A small but consistent number of patients have normal electrodiagnostic data early in their illness and others are abnormal but without diagnostic features of demyelination. This latter situation is most evident in the group of patients with absent or markedly reduced distal CMAP amplitudes (with normal DLs). Many of these patients have a severe clinical syndrome with profound weakness, protracted respiratory dependency, and a high incidence of later active denervation. While some cases clearly represent severe distal conduction block,9,30,35,51,67,72 others seem to have predominately or exclusively an axonal disease that spans the clinical definition of the GBS.16,25–27 The clinical, pathological, and electrophysiological distinctions between “demyelinating GBS” (acute inflammatory demyelinating polyneuropathy), and “axonal GBS” await future clarifications.

The electrophysiological definition of partial conduction block is another area of considerable interest and importance to the clinical electrodiagnostic medicine consultant. It has been demonstrated clinically14 and experimentally65 to be the most common and consistent marker of a demyelinating neuropathy but there has been much controversy regarding its electrodiagnostic criteria.21 The recognition that desynchronization of the motor nerve volleys alone can cause marked distal-to-proximal amplitude and area decrements from “phase cancellation” without any element of conduction block sparked the debate.43,57 Phase cancellation occurs when there is a differential slowing of CV in individual motor fibers of a peripheral nerve. Thus, there is an increase in the range of CVs in the population of the fastest conducting myelinated fibers that determine the recorded CMAP. This desynchron-

\[
\begin{array}{|c|c|}
\hline
\text{Table 5. Dutch Guillain–Barré Study Group’s electrodiagnostic criteria for an acute demyelinating polyneuropathy.} \\
\hline
\text{One of the following abnormalities in at least two nerves} \\
1. ↑ distal motor latency >150% of ULN \\
2. ↓ CV <70% LLN \\
3. ↑ F-wave latency >150% of ULN \\
4. Abnormal CMAP amplitude drop (proximal to distal) > ULN \\
5. Abnormal distal CMAP duration: distal CMAP duration >300% ULN \\
6. Abnormal TD: distal to proximal CMAP duration ratio >150% ULN \\
\hline
\end{array}
\]

Adapted from Meulstee J, Van der Meche FGA, and the Dutch Guillain–Barré Study Group.48

↑, increase; ↓, decrease; ULN, upper limit of normal; LLN, lower limit of normal; CV, motor conduction velocity; TD, temporal dispersion; CMAP, compound muscle action potential.
nization of the motor volley can lead to a "cancellation" effect when the negative phase of the slower fibers summates with the positive phase of a faster fiber. This reduces both the amplitude and area of the recorded CMAP. The longer the distance between stimulation points, the greater the effect from the dispersion of the volleys. Several points are worthy of comment:

1. In the early phase of acute demyelinating PNs, motor volley desynchronization is a minor contributor to motor-amplitude decrements but in a more subacute or chronic setting, it can become a major factor, especially with remyelination.
2. Phase cancellation occurs over long lengths of peripheral nerve; a significant, discrete segmental amplitude and/or area decrease is most likely a true partial conduction block.
3. Temporal dispersion is another affect of desynchronization of the motor volley and usually accompanies phase cancellation.
4. Both significant temporal dispersion with desynchronization and phase cancellation (potential range: 20–50% proximal amplitude or area decrement) and partial conduction block are electrophysiological signs of demyelination and for most practical purposes have the same diagnostic implications.

Although the initial study of the patient discussed here suggested a demyelinating PN, the later studies contain many more demyelinating features and this is a consistent feature in the literature. Decreases in CVs and increases in DLs in later studies are common in the main segments of nerves tested with conventional motor NCSs. This could be due to an increase in the number of demyelinated regions along the course of the tested segment, the decreased CV in remyelinated segments, or a combination of both.

The needle EMG examination, in contrast, tends to be of limited value in GBS. Later in the illness, the combination of near-normal motor amplitudes, reduced motor unit recruitment, and absent denervation potential strongly suggests a demyelinating mechanism; however, early in the illness, this pattern is also consistent with proximal axonal damage with pending wallerian degeneration. Early profound denervation potentials suggest a significant component of axonal damage; however, some degree of active denervation is common in severe, otherwise typical, demyelinating GBS, presumed due to some secondary axonal damage. Myokymic discharges can be seen in limb and face muscles and carry no diagnostic or prognostic significance.

There have been a few electrodiagnostic features that appear to be useful to predict the course of GBS except the CMAP amplitude. A marked amplitude reduction (<20% of the lower limits of normal) is indicative of a long and incomplete recovery. It has been suggested that comparing a patient’s own sequential NCSs has greater predictive power. The best clinical prognosticator has been the rapid evolution of the weakness and/or ventilator dependency (poorer outcome). It is interesting that in recent studies, the density of fibrillations or positive sharp waves have not correlated with prognosis while earlier authors suggested increased active denervation was a poor prognostic sign independent of CMAP amplitude.

When confronted with a suspected GBS patient, every attempt should be made to identify regions of conduction block. The highest diagnostic yield can be obtained by: (1) increasing the number of nerves examined; (2) examining the longest possible nerve segments; (3) focusing on the study of weak muscles; (4) using ancillary procedures such as blink reflexes, phrenic nerve conduction, or root stimulation to examine the most affected regions; and (5) exploring the context of certain abnormalities. For example, in this case, the absence of tibial F waves with reduced recruitment of motor units and a new normal CMAP amplitude is strongly suggestive of a proximal, partial conduction block. Additionally, the normal sural SNAP amplitude in combination with reduced or absent upper-extremity sensory amplitudes is commonly seen in demyelinating PNs and conversely is uncommon in axonal PNs. Lastly, the examination of the waveforms themselves can add useful information. This may require altering the conventional sensitivity and duration CMAP recording settings to expand the late components. The tibial CMAP shown in Figure 2 has a prolonged duration but it is the small dramatically dispersed components that define the abnormality as demyelination if present early in the illness (before the time reinnervation could occur).

In conclusion, NCSs are an excellent resource in the evaluation of a patient with the clinical diagnosis of GBS. By selecting the electrophysiological approach based on the clinical features, both the sensitivity and specificity of the test are enhanced.

REFERENCES

1. Ad Hoc Subcommittee of the American Academy of Neurology AIDS Task Force. Criteria for diagnosis of chronic inflam-


