



# Diagnostic Criteria and Serial Nerve Conduction Study for Guillain-Barré Syndrome Subtype Diagnosis

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## ABSTRACT

The nerve conduction study (NCS) is a helpful test used for identifying Guillain-Barré syndrome (GBS) subtypes. However, the comparison of values between single and serial NCS has not been well documented. To evaluate the current electrophysiological criteria for the diagnosis of GBS subtypes and to examine the value of single NCS as compared to serial NCS. Retrospective review of 44 patients with GBS from two tertiary hospitals in Thailand. Comparing demyelinating criteria revealed that Albers' criteria had the highest sensitivity (98%) and Cornblath's criteria had the lowest (53%). Ten percent of patients were reclassified from demyelinating to axonal subtypes after a second NCS. In addition, the demyelinating pattern was more prevalent in the tibial, peroneal and median nerves. Albers' criteria had the greatest sensitivity for diagnosing GBS. Performing additional NCS would increase diagnostic accuracy and, as a minimum, the tibial, peroneal and median nerves should be tested.

**Keywords:** Electrophysiological diagnostic criteria; Electrophysiological study; Guillain-Barré syndrome; Guillain-Barré subtype; Nerve conduction study

## 1. Introduction

Guillain-Barré syndrome (GBS) is an acute, immune-mediated neuropathy that is classified into demyelinating and axonal subtypes.

The diagnosis of GBS is based on clinical characteristics and supporting laboratory investigations [1, 2]. Electrophysiology (nerve conduction study; NCS) is helpful for

identifying subtypes, rates of progression and severity, as well as predicting prognosis [3, 4].

The aim of this study was to evaluate the current electrophysiological criteria for the diagnosis of GBS subtypes, to correlate the clinical course with the electrophysiological findings and to examine the value of single and serial NCS changes.

## 2. Materials and Methods

### 2.1 Study design

This was a retrospective study of GBS patients admitted to either the Thammasat University Hospital (TUH) or the Bangkok Hospital Medical Center (BMC) from the 1<sup>st</sup> of January, 2009 to the 31<sup>st</sup> of October, 2017. The study was approved by the Ethics Committees of TUH and BMC.

### 2.2 Data collection

Inclusion criteria: Patients who were 15 years of age or older who had been admitted to TUH or BMC with GBS and had at least one NCS. The diagnosis of GBS and its subtypes were based on clinical criteria and the Brighton criteria, which were confirmed by the treating neurologists [1].

Exclusion criteria: Patients who had a chronically progressive course for more than 8 weeks, whose diagnosis was not GBS e.g., acute onset of chronic inflammatory demyelinating polyneuropathy (CIDP), or whose GBS recording file was missing data.

### 2.3 Clinical neurophysiology

NCSs of the upper and lower limbs were performed on the median, ulnar, tibial, peroneal and sural nerves. The measured parameters were compound motor action potential (CMAP), sensory nerve action potential (SNAP), conduction velocity (CV), distal motor latency (DML), F-wave latency, the presence of temporal dispersion (TD) and the proximal to distal amplitude ratio (conduction block; CB).

Skin temperature was controlled to be at least 32° C. Serial NCSs were divided into

3 periods; 0-1, 2-3 and more than 4 weeks after onset of symptoms.

Demyelinating subtype criteria used were from Albers 1985, Cornblath 1990, Ho 1995 and Hadden 1998. Axonal subtype criteria used were from Ho 1995 and Hadden 1998. [5]. Combining all of the data, patients were grouped as follows: (i) demyelinating subtype: if  $\geq 2$  nerves showed demyelinating features on the motor NCS, (ii) axonal subtype: based on an unrecordable or reduced CMAP on the motor NCS with no more than one demyelinating feature in any nerve, (iii) mixed subtype: if demyelinating and axonal injury were both present and (iv) equivocal: if the NCS results did not meet any of the NCS criteria above.

### 2.4 Statistical analysis

Analyses were performed using SPSS v.24 (Armonk, NY). Categorical data are described as frequencies; continuous data are described as means, ranges and standard deviations (SDs). The measured probability of agreement between different diagnostic NCS criteria was analyzed by the kappa value.

## 3. Results and Discussion

### 3.1 Demographic and clinical characteristics

During the study period, 44 patients fulfilled the criteria for GBS with characteristics that are summarized in Table 1. The majority of patients were Asian (59.1%). Twenty-five percent of patients had diabetes mellitus as an underlying disease; all of these patients had less than 5 years of disease duration and had already been examined to rule out diabetic neuropathy.

**Table 1.** The general characteristics of the 44 patients with Guillain-Barré syndrome.

		<b>Number of patients</b>	<b>Percent (%)</b>
<b>Gender</b>	Male	21	47.7
	Female	23	52.3
<b>Age (mean ± SD)</b>		49.2 ± 17.7	
<b>Nationalities</b>	American	2	4.5
	Asian	26	59.1
	European	7	15.9
	South African	2	4.5
	Others	7	15.9
<b>Level of diagnosis*</b>	1	23	52.3
	2	15	34.1
	3	6	13.6
	4	0	0
<b>Diagnostic subtypes</b>	AIDP	28	63.6
	AMAN	7	15.9
	AMSAN	1	2.3
	MFS	5	11.4
	PCB	3	6.8
<b>Underlying diseases</b>			
	Diabetes mellitus	11	25
	Hypertension	13	29.5
	Dyslipidemia	11	25
	Human immunodeficiency virus	0	0
<b>Alcohol consumption</b>		4	9.1
<b>Recent infection and immunization</b>			
	Upper respiratory tract infection	7	15.9
	Diarrhea	9	20.5
	History of vaccination	0	0
<b>Signs and symptoms</b>			
	Motor symptoms	32	72.7
	Sensory symptoms	23	52.3
	Ataxia	8	18.2
	Autonomic symptoms	5	11.4
	Facial weakness	7	15.9
	Ophthalmoplegia	3	6.8
	Diplopia	4	9.1
	Ptosis	5	11.4
	Speech problems	9	20.5
	Bulbar weakness	7	15.9
	Hyporeflexia or Areflexia	40	90.9
<b>Admission Length (day)</b>		<b>Days</b>	
	Length of hospital stay (mean ± SD)	15.8 ± 12.7	
	Length of ICU stay (mean ± SD)	3.5 ± 0.8	
	Duration (days)	1 - 49	
	Respiratory support (No. of patients)	8	18.2

\*Level of diagnosis, "Brighton criteria" ranging from level 1 (highest level of diagnostic certainty) to level 4 (possibly due to insufficient data for further classification); AIDP, acute inflammatory demyelinating polyradiculoneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy; MFS, Miller Fisher syndrome; PCB, pharyngo-cervical-brachial variant of GBS.

### 3.2 Serology and cerebrospinal fluid (CSF) analysis

A lumbar puncture (LP) was performed in 30 (68%) patients, on average 6.6 days (range 1-30 days) after symptom onset. Albuminocytologic dissociation (elevation of CSF protein > 0.55 g/L without an elevation in white blood cells) was found in 18 (60%) patients. Serology for anti-ganglioside antibody was performed in 13 (29.5%) patients; of these 13 patients, 1 was positive for anti-GQ1b. This patient also had Miller Fisher syndrome (MFS).

### 3.3 Nerve conduction studies

The time to perform an NCS after the onset of symptoms ranged from 1 to 30 days, with the mean being 7.8 days. The number of demyelinating and axonal GBS subtypes are summarized in Table 2. Albers' criteria had the highest (98%) sensitivity and Cornblath's criteria had the lowest (53%) for defining the demyelinating pattern.

**Table 2.** Guillain-Barré syndrome subtypes based on demyelinating and axonal criteria.

	Albers	Cornblath	Ho	Hadden
<b>Demyelinating</b> (N=47)	46 (98%)	25 (53%)	44 (94%)	43 (91%)
<b>Axonal</b> (N=3)			3 (100%)	2 (67%)

"N" represents the number of results classified in each subtype for all performed NCS.

The degree of agreement (kappa values) among these neurophysiological diagnostic criteria was calculated. When using Hadden criteria as a reference, the highest positive correlation was seen in Albers' criteria (Kappa value 0.78) and the lowest correlation in Cornblath's criteria (Kappa value 0.44).

A total of 20 patients had more than 1 NCS performed; the subtype classification was changed in 2 patients from demyelinating to axonal subtype (patient No.15 and 34, Appendix 1).

The demyelinating neuropathy pattern was found more frequently in the peroneal

nerves, followed by the tibial, median and then ulnar nerves. Moreover, the axonal neuropathy pattern was found more often on lower limb nerves (tibial and peroneal nerves) as shown in Appendix 2a and 2b.

In the upper limbs, abnormalities of conduction velocity, distal motor latency, temporal dispersion and F-wave latency were detected more frequently in the median nerve than the ulnar nerve, whereas conduction block was more frequently detected in the ulnar nerve. In the lower limbs, abnormalities of conduction velocity, distal motor latency and temporal dispersion were identified more frequently in the peroneal nerve whereas conduction block and prolonged F-wave latency were more common in the tibial nerve (Appendix 3).

Sural sparing pattern was a common finding in GBS patients, ranging from 80-96% in AIDP and 67-100% in AMAN subtypes (Appendix 4).

In fact, our findings are both similar to, and build on, findings from studies by others [6-9]. We also found that the diagnostic sensitivity of Albers' criteria was highest (98%) for detecting the demyelinating pattern, whereas Cornblath's criteria had the lowest sensitivity (53%). The difference between Albers' and Cornblath's criteria has also been documented in previous studies which have reported variable sensitivities ranging from 64-82% and 21-39% for Albers' and Cornblath's criteria, respectively [5]. This could possibly be due to the lower threshold of demyelination in Albers' criteria.

In our series, just under half of the 44 patients (45.5%) had more than one NCS and this resulted in a change in diagnosis in 2 patients, from demyelinating in the acute phase of the disease to an axonal subtype later on after disease progression had begun. This has been reviewed by others and the incorrect early classifications might have resulted from rapidly reversible or slowing conduction block, called reversible conduction failure (RCF) [5, 10]. When conduction block promptly resolved, DML and CMAP

amplitudes rapidly returned to normal values without developing TD. These changes may be related to antibody deposition at the nodes of Ranvier, resulting in the detachment of paranodal myelin, which the NCS detects as paranodal demyelination even though the primary pathology is in the axon [11, 12].

These altered conduction velocity and conduction block readings appeared to be the two major abnormal parameters in the lower limb nerves of the demyelinating subtype (Appendix 3); however, F-wave prolongation was much less common. The peroneal nerves were the most frequently affected in both the demyelinating and axonal GBS subtypes, followed by the tibial and median nerves. In addition, the ulnar nerve was less commonly affected in both GBS subtypes.

These findings are in contrast with those of previous studies (Table 3) [6]. In one study from Birmingham, UK (2001-2012), the authors retrospectively analyzed the NCS data of 97 GBS patients. They showed that common peroneal and median nerves were the most commonly affected in AIDP, while the tibial nerve was the most frequently affected in the axonal subtype. Furthermore, conduction block and DML prolongation were the main abnormal parameters in AIDP. On the other hand, the following features were consistent with our study: CV and CB were more pronounced in the lower limbs, DML was more prevalent in the upper limbs and F-wave prolongation was significantly less common. Therefore, we propose that the minimum NCS protocol for GBS diagnosis should include three nerves: the peroneal, tibial and median nerves, which will provide the highest yield for GBS detection.

For AIDP, assessment should focus on CV, CB and TD in the lower limbs and the DML should be the focus in the upper limbs. In axonal GBS, CMAP amplitude reduction is often present in the lower limbs. Performing NCS on admission and 2 - 4 weeks after symptom onset will help to confirm the acute neuropathy and improve subtype classification [13]. Importantly, thorough evaluation

that focuses on obtaining complete information on multiple nerves from the arms and legs is extremely crucial to establish an accurate diagnosis.

**Table 3.** Differences in the findings of commonly affected nerves between this study and that of Rajabally et al. [6].

		Previous study	This study
<b>Demyelinating subtypes</b>	Upper limbs	Median nerves (DML)	Median nerves (DML)
	Lower limbs	Peroneal nerves (CB)	Peroneal nerves Tibial nerves (CB, Reduced CV)
<b>Axonal subtype</b>		Tibial nerves	Peroneal nerves Tibial nerves

DML, distal motor latency; CB, conduction block; CV, conduction velocity.

This study had a number of limitations. It was retrospective, so some data were missing for some patients. The data were collected from two different hospitals, which used different laboratories and electrophysiological equipment but this issue was resolved by using the reference values, set by American Association of Neuromuscular & Electrodiagnostic Medicine [AANEM] in 2016 [14].

#### 4. Conclusion

This retrospective study has provided functional data on GBS in the local Thai and non-Thai populations. It has also led to a simple and practical protocol for diagnosing GBS: 2 NCS examinations 2-4 weeks apart examining the peroneal, tibial and median nerves. The Albers' criteria should be used for diagnosing demyelinating GBS. Abnormalities of CV, CB and TD in the lower limbs are the best criteria for investigating demyelinating GBS while CMAP amplitudes are the best criteria for axonal GBS.

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## Appendix

### Appendix 1. Guillain-Barré syndrome subtypes based on clinical and electrophysiological studies at different time intervals in 44 patients.

Patients No.	Clinical diagnosis (first visit)	Electrophysiology diagnostic subtypes		
		week 0-1	week 2-3	week $\geq$ 4
1	AIDP	Equivocal	-	Demyelinating
2	AIDP	Mixed	Demyelinating	Demyelinating
3	AIDP	-	Demyelinating	-
4	AIDP	Demyelinating	-	-
5	AIDP	Demyelinating	-	-
6	AIDP	Demyelinating	Demyelinating	Demyelinating
7	AIDP	Demyelinating	Demyelinating	-
8	AIDP	-	Demyelinating	-
9	AIDP	Demyelinating	-	-
10	AIDP	Equivocal	-	Demyelinating
11	AIDP	Demyelinating	Demyelinating	Demyelinating
12	AIDP	Mixed	Demyelinating	-
13	AIDP	Demyelinating	-	-
14	AIDP	-	Demyelinating	-
15	AIDP	Demyelinating	Axonal	-
16	AIDP	Mixed	Demyelinating	-
17	AIDP	Equivocal	Demyelinating	-
18	AIDP	Demyelinating	-	Demyelinating
19	AIDP	Demyelinating	-	-
20	AIDP	Mixed	Demyelinating	-
21	AIDP	Demyelinating	-	Demyelinating
22	AIDP	Demyelinating	-	-
23	AIDP	Demyelinating	-	-
24	AIDP	Demyelinating	Demyelinating	-
25	AIDP	-	Demyelinating	-
26	AIDP	Demyelinating	Demyelinating	-
27	AIDP	-	Demyelinating	-
28	AIDP	Equivocal	-	-
29	AMAN	Demyelinating	-	-
30	AMAN	-	Demyelinating	-
31	AMAN	Demyelinating	-	-
32	AMAN	Equivocal	Demyelinating	-
33	AMAN	Equivocal	-	-
34	AMAN	Equivocal	Demyelinating	Axonal
35	AMAN	-	Demyelinating	-
36	AMSAN	Mixed	Equivocal	-
37	MFS	Demyelinating	-	-
38	MFS	Equivocal	Equivocal	-
39	MFS	-	-	Equivocal
40	MFS	-	Demyelinating	-
41	MFS	Demyelinating	-	-
42	PCB	-	Demyelinating	-
43	PCB	Equivocal	Axonal	-
44	PCB	Equivocal	-	-

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy; PCB, pharyngeal-cervical-brachial weakness; MFS, Miller-Fisher syndrome.

**Appendix 2a:** Frequency of motor nerve abnormalities according to demyelinating criteria.

Nerves	Demyelinating criteria			
	Albers	Cornblath	Ho	Hadden
	46*	25*	44*	43*
Lt median	28 (61%)	9 (36%)	25 (57%)	26 (60%)
Rt median	33 (72%)	11 (44%)	27 (61%)	29 (67%)
Lt ulnar	23 (50%)	6 (24%)	15 (34%)	20 (47%)
Rt ulnar	27 (59%)	7 (28%)	18 (41%)	19 (44%)
Lt tibial	40 (87%)	15 (60%)	26 (59%)	28 (65%)
Rt tibial	38 (83%)	11 (44%)	28 (64%)	29 (67%)
Lt peroneal	41 (89%)	12 (48%)	43 (98%)	33 (77%)
Rt peroneal	44 (96%)	14 (56%)	44 (100%)	34 (79%)

\* The total number of demyelinating or axonal GBS subtype were diagnosed by those criteria.

**Appendix 2b.** Frequency of motor nerve abnormalities according to axonal criteria.

Nerves	Axonal criteria	
	Ho	Hadden
	3*	2*
Lt median	1 (33%)	0
Rt median	2 (67%)	0
Lt ulnar	0	0
Rt ulnar	1 (33%)	0
Lt tibial	2 (67%)	0
Rt tibial	2 (67%)	0
Lt peroneal	2 (67%)	2 (100%)
Rt peroneal	2 (67%)	2 (100%)

\* The total number of demyelinating or axonal GBS subtype were diagnosed by those criteria.

**Appendix 3.** Frequency of detected abnormal parameters in demyelinating subtypes as a function of the tested nerves.

N=47*	CV	DML	TD	CB	F
Lt median	19 (40%)	16 (34%)	19 (40%)	6 (13%)	5 (11%)
Rt median	27 (57%)	20 (43%)	22 (47%)	7 (15%)	5 (11%)
Lt ulnar	11 (23%)	12 (26%)	12 (26%)	14 (30%)	2 (4%)
Rt ulnar	11 (23%)	13 (28%)	12 (26%)	12 (26%)	2 (4%)
Lt tibial	22 (47%)	11 (23%)	15 (32%)	26 (55%)	3 (6%)
Rt tibial	21 (45%)	11 (23%)	16 (34%)	26 (55%)	3 (6%)
Lt peroneal	32 (68%)	12 (26%)	23 (49%)	20 (43%)	1 (2%)
Rt peroneal	36 (77%)	10 (21%)	23 (49%)	26 (55%)	1 (2%)

\*N = total number of demyelinating subtype results  
 CV, conduction velocity; DML, distal motor latency; TD, temporal dispersion;  
 CB, conduction block; F, F-wave latency.



**Appendix 4.** Frequency of sural sparing pattern in each Guillain-Barré syndrome subtypes.

<b>Number of</b>	<b>Albers</b>	<b>Cornblath</b>	<b>Ho</b>	<b>Hadden</b>
<b>Demyelinating cases</b>	46	25	44	43
- Sural sparing	37 (80%)	24 (96%)	38 (86%)	38 (88%)
<b>Axonal cases</b>			3	2
- Sural sparing			2 (67%)	2 (100%)