Patterns and severity of conduction abnormalities in Guillain-Barré syndrome

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Abstract

Whether the conduction abnormalities and lesions underlying them are randomly distributed throughout the peripheral nervous system (PNS) or certain regions are selectively more vulnerable to attack is an unresolved question in Guillain-Barré syndrome (GBS). To examine this question, 15 cases of GBS were comprehensively examined using electrophysiological techniques which allowed close examination, quantitation and comparison of conduction abnormalities in motor and sensory fibres of the upper limb between the spinal cord and the distal extremities of the nerve fibres. Comparison of these studies with results expected in a model where the chances of conduction failure were uniformly distributed led to the conclusion that conduction slowing and block were not uniformly distributed in most cases. Conduction block was maximal in the terminal segment distal to the wrist and to a lesser extent both conduction block and conduction slowing were disproportionately greater across the elbow and in the axillary to spinal root segments in over one half of the cases. These findings support the hypothesis that certain regions, perhaps because of relative deficiencies of the blood-nerve barrier, may be more vulnerable in GBS than other regions.

One question still unresolved in Guillain-Barré syndrome (GBS) is whether lesions underlying the conduction abnormalities in this disease are uniformly distributed throughout the peripheral nervous system (PNS) or certain regions consistently bear the brunt of the attack. Previous studies have suggested that the conduction abnormalities might be uniformly distributed, a conclusion based on close matches between actual changes in maximum "M" potential amplitudes, between successively more proximally displaced stimulus sites and what might be expected from a model where conduction block was uniformly distributed throughout the PNS.^{1,2} Other studies suggested conduction block might not be uniformly distributed but rather, greater in the distal terminal and proximal segments of the PNS and across common sites of entrapment.³⁻⁶ The latter hypothesis might suggest selective vulnerability of the PNS in regions where the blood-nerve barrier is considered to be

relatively deficient,⁷⁻¹⁰ and as a consequence affording less protection from circulating cellular and humoral agents in the disease.

Our study was designed to assess patterns of conduction abnormalities throughout the course of motor fibres between the spinal roots and their target muscles and sensory fibres between the spinal cord and digits.

Methods

Subjects

Fifteen patients with clinically defined GBS¹¹ were studied, and their clinical states at peak disability graded.¹² Two patients (8 and 15) briefly relapsed following a course of plasma exchange.

Approval from the Human Experimentation Committee of the University of Western Ontario was obtained for the study and informed consent obtained from all patients.

Electrophysiological studies

Motor conduction studies

Surface electrodes (DANTEC) in a belly-tendon configuration were used to record the maximum hypothenar "M" potential. The ulnar nerve was stimulated using bipolar surface electrodes at the wrist, at least 2 cm distal to the cubital tunnel, 2-3 cm proximal to the elbow, and as high in the axilla as possible.

A DEVICES D-180 high voltage stimulator was employed to stimulate the spinal roots. The anode was positioned 1-2 cm lateral to the tip of the C6 spine and the cathode directly inferiorly. Manually triggered single pulses were used to keep to a minimum the number of stimuli required to establish a supramaximal response (five or fewer usually). Most patients judge stimulation of the spinal roots in this manner as no more uncomfortable than supramaximal stimulation of nerve trunks elsewhere, provided care is taken to use carefully graded single pulses and the procedure explained beforehand.

In controls and patients there was no appreciable volume conduction to the hypothenar recording sites from median supplied intrinsic hand or forearm muscles. This was important, as selective stimulation of ulnar nerve fibres is impossible at the spinal root or even axillary sites.

As the central objective of this study was to assess the overall severity and distribution of conduction slowing and block between the spinal cord and distal terminations of the nerve fibres, comparisons were made between the fifteen GBS cases and controls for:

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Received 12 March 1990 and in final revised form 22 November 1990
Accepted 6 December 1990

1) "Overall" percentage reductions in maximum "M" potential negative peak area ("M"A) between the spinal roots and motor point.

This was calculated by:

$$\frac{("M")A_{MP} - ("M")A_{SR}}{("M")A_{MP}} \times 100$$

where $("M")A_{MP}$ and $("M")A_{SR}$ = maximum hypothenar "M" potential negative peak area at the motor point and spinal roots respectively. As "M"A is more independent of interpotential phase cancellation than amplitude, "M"A was chosen as better reflecting conduction block.

In eight controls, a needle electrode, insulated to within 2–3 mm of its tip was inserted as close to the motor point as possible and supramaximal stimuli used to evoke a maximum hypothenar "M" potential. This technique, however, was sometimes uncomfortable and precluded direct study of the terminal 5–15 mm of the nerve. A reasonable substitute for such a directly obtained value for the motor point hypothenar maximal "M" potential was therefore required if conduction in the terminal segment between the wrist and hypothenar motor point was to be assessed in our patients. As a practical alternative to needle stimulation near the motor point we elected to substitute the control mean –2 SD value for the maximum hypothenar "M"A at the wrist for the motor point value in the patients. This was considered a reasonable compromise as hypothenar "M"A values in response to near motor point stimulation were within 5% of one another in eight controls (fig 1).

While choice of the –2 SD value might have underestimated reductions in "M"A in

the terminal segment in some cases, we considered the choice a better alternative to possibly over estimating terminal reductions in "M"A in other patients had we chosen the control mean or mean –1 SD values.

In GBS patients overall percentage reductions in "M"A between MP and SR were calculated as follows:

$$\frac{\text{Control } ("M")A_{MP} - \text{GBS } ("M")A_{SR}}{\text{Control } ("M")A_{MP}} \times 100$$

where control $("M")A_{MP}$ = the mean –2 SD for the control "M"A at the wrist, and GBS $("M")A_{SR}$ = "M"A evoked by stimulation of the spinal roots in the patient.

2) Percentage reductions in "M"A between the wrist and motor point

This was calculated by:

$$\frac{\text{Control } ("M")A_{MP} - \text{GBS } ("M")A_w}{\text{Control } ("M")A_{MP}} \times 100$$

where GBS $("M")A_w$ = the "M"A evoked by stimulation at the wrist in the patient.

3) Percentage reductions in "M"A per 10 millimetre (mm) length of nerve for each successively more proximal segment between the motor point and spinal roots

As quantitative assessment of conduction block in more proximal segments is conditioned by conduction in distal segments, the motor point value for the GBS patients served as the denominator for calculating percentage reductions in "M"A for successively more proximal segments. Moreover, as the distances for the various segments were not equal, reductions in "M"A were adjusted to a standard distance, here 10 mm, calculated by:

$$\frac{("M")A_{\text{distal}} - ("M")A_{\text{proximal}}}{\text{Control } ("M")A_{MP}} \times \frac{10}{d} \times 100$$

where $("M")A_{\text{distal}}$ and $("M")A_{\text{proximal}}$ = "M"A values elicited by supramaximal stimulation at the distal and proximal stimulus sites for each segment.

4) The motor terminal latency in milliseconds (ms) in the terminal segment and maximum motor conduction velocities in metres per second (M/s) for each successively more proximal segment.

Conventional techniques were employed for measuring the motor terminal latency (MTL) to the hypothenar muscles and maximum motor conduction velocities (MMCVs) across the forearm, elbow, and proximal arm. The distance between the axillary and cervical (anode) stimulus sites was measured with callipers and the MMCV between these stimulus sites calculated in the conventional manner. All studies were carried out with the elbow extended.

5) Sensory conduction studies

To examine sensory fibres of equivalent diameter to the motor fibres, somatosensory evoked potential studies were carried out on the median nerve. While studies of ulnar sensory conduction would have been preferable,

Figure 1 Maximum hypothenar "M" potentials recorded with surface electrodes in response to supramaximal percutaneous stimulation at the wrist, below the elbow, above the elbow, axilla and spinal roots in a control. Additionally, a monopolar needle electrode was inserted as close to the hypothenar motor point as possible and a supramaximal stimulus delivered through the needle (anode was a surface plate over the back of the hand). No significant differences between maximum "M" potentials elicited by stimulation at the motor point and wrist were seen in this or seven other controls.

cervical potentials with the latter were simply too poorly defined to allow accurate identification of the onset in controls and patients.

Percutaneous stimuli at the wrist were adjusted to evoke maximal antidromic sensory nerve action potential and sensory conduction velocities (MSCVs) between the wrist and digits, wrist to axilla, and axilla to spinal cord calculated and the latency to the N₂₀ potential measured. Orthodromic nerve trunk potentials were recorded as high in the axilla as possible with the reference electrode positioned over the lateral deltoid. The latter potentials no doubt include antidromic potentials in motor fibres as well as orthodromically conducted potentials in sensory fibres. The cervical potential was recorded over the C6 spine with FZ as reference. Additionally, the cortical evoked potential was recorded over the primary sensory area for the hand, again with FZ as reference. Surface electrodes were used throughout to record these potentials except for a bare needle electrode for the scalp recording. The latter provided a convenient low resistance (less than 2k ohms) relatively painless electrode with which to record from the hairy scalp. The ground was placed about the proximal forearm. All patients were examined as close to peak disability as possible.

Results

Motor conduction

Controls: "M" potential size and motor conduction velocities

In the controls the maximum hypothenar "M" potential negative peak areas (1 SD) in millivolts milliseconds (mV ms) at the wrist and spinal roots were 37.2 (7.3) and 32.4 (7.7) mV ms respectively, the maximum reduction in any control being 23.9% between the wrist and spinal roots. For comparison, the maximum

Figure 2 Hypothenar maximum "M" potential recordings from patient 4 studied at five days illustrating the pattern of reductions in "M" potential size. At this stage the overall reduction in "M" A between the motor point (control wrist - 2 SD) and spinal roots was 96.9%, while that between motor point and wrist was 68%. This case represents a clear example where conduction abnormalities were maximal across the terminal elbow and axillary to spinal root segments. For example, reductions in "M" A per 10 mm of nerve were 9.7, 0.0, 0.6, 0.0, and 0.9 across the terminal forearm, elbow, proximal arm and axillary to spinal root segments respectively. Furthermore, the MMCV between the axilla and spinal roots was 37.2 M/s, a value clearly slowed relative to the proximal arm (58.8 M/s) and relatively normal MMCVs for the elbow and forearm of 44.3 and 49.8 M/s respectively.

Figure 3 Sensory conduction study in case 4 at five days. At this time conduction between the wrist and axilla was normal (MSCV 62.2 M/s and the amplitude of the axillary potential 12.5 µV), distal conduction, however, was characterised by a reduced antidromic sensory nerve action potential from digits II and III (5.6 µV) and proximal conduction was slowed between the axilla and spinal cord (42.4 M/s).

Top two traces: Contralateral cortical evoked potential on two time scales. The configuration and latency to N₂₀ (20.4 ms) were within the normal range but with recovery shortened to 19.5 ms.

Middle trace (cervical recording): gain 2.5 µV; Second trace from bottom (axillary recording): gain 5 µV; Bottom trace (antidromic recorded sensory nerve action potential from digits II and III): gain 5 µV.

increase in negative peak duration of the maximum hypothenar "M" potential between the wrist and spinal roots of any control was 60.1% [mean (1 SD) 14.2 (9.2) fig 1]. MMCVs (1 SD) for hypothenar motor fibres across the forearm, elbow, proximal arm and axillary to spinal root segments respectively were 61.4 (5.2), 52.8 (9.9), 60.5 (6.1) and 75.7 (7.1) M/s, and the hypothenar MTL 2.6 (0.4) ms. The mean MMCV across the elbow was 13.4% less than the mean of the forearm and proximal arm combined, the slowest conduction velocity across the elbow in 20 controls being 37.5 M/s.

GBS patients

Overall and terminal reductions in "M" A

Table 1 illustrates the overall percentage reductions in "M" A between the motor point and spinal roots and between the motor point and wrist at the time of maximal reductions in "M" A. The former exceeded 90% in six and 50% in 12 of the 14 patients. The latter exceeded 50% in five and 20% in nine cases. In five cases, "M" A at the wrist exceeded the control mean - 2 SD value. The changes in "M" A were unaccompanied by any significant increase in negative peak duration at the spinal root level, the increase being less than 20% in 10 cases and in all others less than the maximum seen in any control.

Comparison of reductions in "M" A over successively more proximal segments

Disproportionate reductions in "M" A per 10 mm of nerve across the terminal, elbow and

Table 1 Clinical characteristics and magnitude of reductions in "M" A in GBS patients

Patient	Age (Years)	Time Onset to Peak Weakness (Days)	Clinical Grade at Peak	Percentage Reduction in "M" A		Percent Increase in Negative Peak Duration
				Overall MP-SR	Terminal MP-W	
1	52	4	4	83.6	48.7	0.0
2	20	5	4	87.1	39.8	-2.0
3	48	4	4	83.1	43.8	+6.8
4	23	14	5	96.9	68.1	-12.2
5	32	7	5	89.3	32.7	0.0
6	40	21	5	25.3	0.0	+54.9
7	25	19	4	95.1	4.9	+25.3
* 8	32	21	4	91.9	0.0	+45.0
9	16	10	4	97.8	97.8	+15.9
10	62	17	5	95.6	69.0	-14.4
11	20	20	4	22.9	0.0	+9.5
12	33	9	3	57.8	0.0	+13.5
13	33	6	2	8.8	0.0	+5.8
14	63	3	5	100.0	100.0	?
*15	57	7	3	84.0	34.0	+7.4

Clinical and electrophysiological features of GBS patients.

Percentage reductions are shown in "M" A relative to the motor point, both overall between the motor point and spinal roots and in the terminal segment between the motor point and wrist. Also shown are the percentage increases in negative peak duration for each subject at the spinal root compared with wrist stimulus sites.

Where MP = Motor point

SR = Spinal root

W = Wrist

* = Relapse of GBS briefly following course of plasma exchange.

axillary to spinal root segments in excess of adjacent segments were present in five cases (cases 2, 3, 4, 5 and 15), the terminal and elbow segments in one case (case 10 where spinal root stimulation was not carried out), elbow and axillary to spinal root segments in two cases

(cases 7 and 12), and proximally in one case (case 6).

In most of the preceding cases there were accompanying disproportionate reductions in MMCV or prolongations in MTL in excess of adjacent segments (table 2). Also, reductions in MSCV between the axilla and spinal cord were present in cases 4, 5, 6, 7 and 12 in the face of normal MSCVs between the axilla and wrist. Furthermore, antidromic digital sensory nerve action potentials were reduced in amplitude in cases 3, 4, 6 and 9, or absent in cases 5, 7 and 12, while at the same time the axillary nerve trunk potential exceeded the control lower limiting value (5 mV) in all but one of the same cases (table 3).

In cases 1, 8, 11 and 13 there was no apparent pattern to the reductions in "M" A. Indeed, in cases 13 there was no significant overall reduction in "M" A between the spinal roots and motor point. In case 14 no responses from the hypothenar or thenar muscles could be elicited by stimulation at the wrist although very small "M" potentials (less than 1.0 mVms) could be obtained by stimulation closer to their respective motor points. This case fits all the criteria for "axonal" GBS.¹³⁻¹⁵

Even in the cases where there was no

Table 2 Changes in Motor Terminal Latency and Maximum Motor Conduction Velocity in GBS Patients at the Time of Peak Reduction in "M" A

Subject	Terminal	Forearm	Elbow	Proximal Arm	Axilla to Spinal Root
1	++	+++	+++	++	Complete Block
2	++	+	++	-	+++
3	+	+++	+++	++	+++
4	+++	+	+++	+	+++
5	+	+	-	+	+++
6	-	-	-	-	++
7	-	-	-	-	+
8	+	++	+++	++	+++
9	-	-	-	-	+
10	+	-	+++	-	Complete Block
11	-	-	-	-	-
12	+	-	-	-	+
13	-	-	-	-	-
*14	+++	-	-	-	-
15	-	-	++	+	N/A

MTL (ms)

Normal

3.5-5.0

5.0-10.0

10.0-15.0

>15

*Axonal case

MMCV (M/s)

Normal

<Mean -2 SD

30-40

20-30

<20

Table 3 Sensory conduction

Normal values	Amplitude antidromic digits II and III μV	Terminal MSCV M/s	Wrist-Axilla MSCV M/s	Amplitude axilla μV	Axilla to spinal cord MSCV M/s	Amplitude cervical μV	Cortical	
							Latency ms	Amplitude mV
Mean (ISD)	22.9 (12.4)	58.7 (7.2)	63.9 (5.3)	11.1 (5.1)	60.9 (7.6)	2.2 (0.8)	20.2 (1.2)	4.8 (2.4)
Least control value	7.1							
Patients (Days 1-7)								
3	3.0	46.0	70.0	8.9	53.8	1.1	N/A	N/A
4		49.9	69.2	12.5	42.4	1.0	20.4	2.3
5	0		70.8	14.0	40.3	3.0	N/A	N/A
6	3.0	51.1	72.0	10.2	37.0	1.4	N/A	N/A
9	1.3	57.9	53.3	12.6	46.7	2.3	N/A	N/A
14	4.4	56.0	64.8	1.0	49.9	1.9	21.1	1.9
Patients (Days 8-14)								
1	0		<.....24.3 M/s.....>			3.0	29.0	0.7
4	0		66.9	5.0	31.3	0.6	N/A	N/A
5	2.0	49.4	70.8	14.0	40.3	3.0	N/A	N/A
7	0		62.2	3.0	30.4	0.5	19.7	2.2
12	0		63.8	4.2	55.0	0.8	21.2	1.4
13	4.0	40.3	65.2	4.9	53.2	2.0	18.6	6.5

Table 4 Percentage reductions in "M" A per 10 mm

Subject	Terminal	Forearm	Elbow	Proximal arm	Axilla to spinal roots
1	6.8	0.4	0.7	0.8	0.4
2	6.1	0.6	1.1	0.0	1.0
3	6.7	0.6	1.5	0.1	0.5
4	9.7	0.0	0.6	0.0	0.9
5	5.5	0.1	2.3	0.9	1.3
* 6	0.0	0.0	0.1	0.4	1.2
7	0.9	1.5	1.9	1.0	1.8
* 8	0.0	2.8	1.1	0.2	0.4
9	12.8	0.0	0.0	0.0	0.0
10	10.6	0.0	3.7	0.0	N/A
*11	0.0	0.5	0.0	0.3	0.2
*12	0.0	0.0	0.4	0.0	1.9
*13	0.0	0.2	0.0	0.3	0.2
†14	16.7	—	—	—	—
15	5.0	0.6	1.1	0.0	1.8

Where *denotes maximum "M" potential at wrist exceeding the control mean—2 SD at the wrist and †denotes the axonal case of GBS where there were no thenar or hypothenar responses to stimulation at the wrist.

apparent pattern to the reductions in "M" A per 10 mm of nerve, motor and sensory conduction studies sometimes revealed disproportionate segmental conduction slowing. For example, in case 8 the MMCV was disproportionately reduced across the elbow and axillary to spinal root segments relative to nearby segments (table 2). Only in cases 1 and 13 was sensory conduction assessed and in the latter it was normal while in case 1 conduction was abnormal throughout, between the digits and spinal cord (table 3).

Discussion

At the outset it might be helpful to consider the theoretical and practical problems presented by assessing the magnitude and distribution of conduction block using the methods employed in this study. In the simple model represented by fig 4 where conduction fails at only one site per fibre, reductions in "M" size expressed either as a percentage of the motor point value or as an absolute value are constant over successively more proximal and equidistant segments.

This is not the case where the frequency of conduction failure is high enough for conduction to fail at more than one site along the course of individual nerve fibres.^{12,16} In the latter case it is the most distal sites of conduction failure in nerve fibres which determine the pattern of changes in "M" size, as the site of stimulation is displaced proximally, not any additional more proximally situated sites of conduction failure. Of course the latter contribute to the overall frequency of conduction failure in the segment in which they reside but their contributions to the "M" potential are masked by the most distal sites of conduction failure in each fibre.

Where the chance of conduction failure is the same for all nerve fibres and sites of failure are randomly distributed between the roots and motor point, the size of the "M" potential at successively more proximally displaced stimulus sites is described by an exponential function such that the size of the maximum "M" potential at any stimulus site distance "d" from the motor point equals: $"M"_{MP} \times e^{-b \times d}$ where $"M"_{MP}$ is the size of the "M" potential at

Figure 4 Simple model comprised of five nerve fibres supplying a muscle from which the maximum "M" potential is recorded on the left. The nerve is divided into five equal segments and stimulated at six sites, beginning at the motor point (S_1) and ending at the spinal roots (S_6). The chance of conduction failure is the same for each fibre and there is a one in five chance of conduction failing in one of the five successively more proximal segments. Sites where conduction failed are shown by the X. Shown below is a plot of the maximum "M" potential size as a percentage of the value at the motor point for each of the successively more proximally displaced sites of stimulation. In this model all fibres make an equal contribution to the maximum "M" potential and have identical conduction velocities. No more than one site of failure per fibre between spinal roots and motor point is present.

the motor point, and "b" the probability of conduction block per unit length of nerve.

The resulting pattern of changes in "M" size in models where conduction block is assumed to be uniformly distributed throughout the PNS^{12,16} is characterised by the steepest reduction in "M" size in the terminal segment and ever diminishing reductions in "M" size over successively more proximal segments for equivalent distances between successive stimulus sites. This is true both for absolute reductions in "M" size and percentage reductions in "M" size per unit length of nerve relative to the motor point value (fig 5).

To bring this model in line with our studies we substituted the control mean - 2 SD value for the hypothenar "M" A at the wrist for the 100% motor point value in the model. Thereafter, values for "M" A were calculated for sites closely corresponding to actual sites of stimulation used in our human studies. Such calculations revealed that failure rates reducing "M" A by more than 50% in the terminal segment were accompanied by "M" A values at the elbow and axillary stimulus sites smaller than the control hypothenar motor unit action potential. However, reductions in "M" A of this magnitude were not seen at the elbow and axillary stimulus sites in any of our cases in the face of equivalent or greater than 50% reductions in "M" A in the terminal segment. This suggested to us that conduction block was not uniformly distributed but greatest in the terminal segment in many of our patients. Factoring in known differences in conduction

Figure 5 (A) Progressive reductions in "M" size as a percentage of the maximum "M" potential at the motor point as the distance between the motor point and site of stimulation was increased from 0 to 100% of the length of the nerve. All motor units were considered to generate motor unit action potentials of equal size and their fibres to conduct with equal velocities. The chance of conduction failure were equal for all fibres and equally distributed for each fibre between the motor point and most proximal site of stimulation. Illustrated are cases where conduction failed in 10, 30, 50, 70 and 90% of fibres per 10% length of nerve. (B) Linear transformation of plots in A. If 100% corresponded to a 30 mV ms maximum "M" potential "M"A, 0.1% would correspond to an "M"A value of 30 μ Vms and 0.01 to 3 μ Vms. As the smallest area for any single hypothenar motor unit action potentials recorded with the same surface electrodes is 25 μ Vms, "M"A values falling below 0.1% clearly fall below the size of any single motor unit action potential.

velocities between motor nerve fibres^{17 18} as well as the biphasic and even triphasic character of hypothenar motor unit action potentials would only serve to further reduce "M"A values at the elbow and axilla in the model. This would further accentuate the differences between the model where conduction failures were assumed to be randomly distributed and actual observations in our GBS patients.

What of the distribution of conduction failures proximal to the wrist? To answer this question the model of randomly distributed

conduction failures described in fig 5 was adapted to allow direct comparison with values observed in our patients. Percentage reductions in "M"A relative to the motor point where adjusted for a standard distance of 1% of the length of the modelled nerve. The 1% value closely approximates the percentage reduction in "M"A per 10 mm of nerve in our patients where the overall distance between the motor point and spinal roots averaged 800 mm. In the model, for failure rates where 30% or more of the fibres were blocked in the terminal segment, percentage reductions in "M"A per 1% length of nerve fall off progressively as would be expected where the risk of conduction failure is similar for all fibres and randomly distributed between the motor point and spinal roots (table 5).

The foregoing pattern, however, was manifestly not the case in our subjects. In six of the latter, disproportionately greater reductions in "M"A per 10 mm length of nerve were observed across the elbow relative to the forearm and proximal arm and between the axilla and spinal roots relative to the proximal arm. This pattern received further support from the motor and sensory conduction studies. Reductions in MMCVs in excess of those in adjacent segments were common across the elbow and axilla to spinal root segments and the MTL often prolonged while the MMCV across the forearm was normal or relatively normal. In several cases the earliest conduction slowing was seen in the axillary to spinal root, elbow and terminal segments. Disproportionate reductions in MMCV across the axillary to spinal root segment relative to the proximal arm and forearm received further support from reductions in MSCV between the axilla and spinal cord relative to the segment between the wrist and axilla.

Based on studies of the F-response, conduction slowing across proximal segments of motor nerves in excess of more distal segments has been shown,³ as well as proximal conduction block early in the disease,¹⁹ findings confirmed by Brown and Feasby^{4 5} and Berger *et al.*⁶

Overall, our studies suggest that the primary conduction abnormalities in GBS, including both reductions in conduction velocity and conduction block, may not, in some cases, be uniformly distributed between the spinal cord and the peripheral terminations of nerve fibres. In many cases conduction was slowest and "M"A most reduced across the terminal, elbow and axillary to spinal cord segments while some cases showed more variable patterns. In the former cases, why should the distal and proximal regions be so preferentially affected? The blood-nerve barrier is known to be relatively deficient at the roots and nerve terminals,⁷⁻¹⁰ and perhaps as others have suggested, preferential access of circulatory toxins, antibodies, lymphocytes or monocytes at these sites could determine the pattern of conduction abnormalities in the early course of the disease.

Reductions in "M"A and conduction velocity across the elbow in excess of changes proximal and distal to the elbow could be explained in two ways. First, these could

Table 5 Percent reductions in "M"A per one percent length of nerve

Percentage nerve fibres blocked per 10% length of nerve	Terminal	Forearm	Elbow	Proximal arm	Axilla spinal roots
90	2.0	0.1	0.0	0.0	0.0
80	1.8	0.1	0.0	0.0	0.0
70	1.6	0.2	0.0	0.0	0.0
60	1.4	0.3	0.0	0.0	0.0
50	1.1	0.3	0.1	0.0	0.0
40	0.9	0.4	0.1	0.1	0.0
30	0.7	0.3	0.2	0.1	0.0

Percentage reductions in "M"A per one percentage length of nerve were calculated for comparison with actual values in GBS patients (table 4). One per cent is approximately equivalent to the 10 mm segment in the patients where overall distances between the hypothenar motor point and spinal root averaged 800 mm. Percentage reductions per one percentage length were calculated for lengths of nerve for the terminal, forearm, elbow, proximal arm, and axilla to spinal root segments, corresponding to 10, 30, 10, 15 and 35 percentage of the nerve between motor point and spinal roots.

simply reflect compression of the ulnar nerve behind the medial epicondyle or in the cubital tunnel in patients unable to adjust the position of their limbs because of paralysis. Alternatively, the blood-nerve barrier may have been compromised at this common entrapment site before the onset of the disease. The latter could render nerves vulnerable to attack at these common entrapment sites, especially early in the disease.

One problem not resolved by this study was determining the relative contributions of conduction block in otherwise intact fibres, conduction block in nerve fibres undergoing degeneration, and axon losses, to the reduction in "M" A in the terminal segment. Nerve fibres crushed severely enough to undergo degeneration retain the ability to transmit impulses distal to the crush for several days before conduction fails and the fibres break down.²⁰ The duration of the biological attack in GBS is unknown and different fibres or indeed different sites on the same fibre could be attacked many days apart. In case 4, however, despite the severe reductions in "M" A with wrist stimulation at 5 (fig 2) and even 18 days, prompt recovery subsequently followed at 32 days strongly suggesting the previous terminal reduction in "M" A was largely explicable by conduction block in demyelinated nerve fibres rather than axonal degeneration. At the other extreme, inexcitable nerve carries the gloomy prospect of substantial axonal degeneration having taken place¹³⁻¹⁵ and unfortunately was subsequently borne out by our case 14.

How well did our studies correspond with the pathology of GBS? Haymaker and Kernohan²¹ examined 50 fatal cases. The interval between the onset of symptoms and the pathological studies varied between two and 46 days. Pathological changes were most evident at the junction between motor and sensory roots and the mixed spinal nerve roots. Lesions tended to be multifocal in distribution, often varying widely in intensity from fascicle to fascicle. However, the PNS distal to the roots was not assessed and intramuscular branches were not studied.

In the study by Asbury *et al*,²² 19 fatal cases were examined. The interval between the onset of symptoms and necropsy was between one day and six years. Nine cases were studied within the first four weeks. Patterns varied from predominant involvement of the roots, with the ventral roots being the more affected, to widespread involvement of roots and peripheral nerve trunks, and still other cases where peripheral nerve trunks themselves were affected with little or no involvement of the roots. In the few cases where intramuscular nerve twigs were examined, striking pathological changes were not often seen. Overall the pattern was quite variable and often multifocal. Unfortu-

nately, their study did not systematically examine all regions between the roots and peripheral terminals of the PNS, nor were quantitative comparisons made of the extent of paranodal and internodal demyelination in different regions of the PNS. The latter is important as the frequency and distribution of inflammatory infiltrates such as these authors emphasised may bear little direct correspondence to sites of conduction failure. The minimum requisite frequency of critically demyelinated fibres to produce striking reductions in "M" A could be as low as 1-3% of affected internodes or paranodal regions, frequencies which could well pass unnoticed even with quantitative studies of teased fibres.

- 1 Van Der Meche FGA, Meulstee J. Guillain-Barré syndrome: a model of random conduction block. *J Neurol Neurosurg Psychiatry* 1988;51:1158-63.
- 2 Van Der Meche FGA, Meulstee J, Vermeulen M, Kievit A. Patterns of conduction failure in the Guillain-Barré syndrome. *Brain* 1988;111:405-16.
- 3 Kimura J. Proximal versus distal slowing of motor nerve conduction velocity in the Guillain-Barré syndrome. *Ann Neurol* 1978;3:344-50.
- 4 Brown WF, Feasby TE. Conduction block and denervation in Guillain-Barré polyneuropathy. *Brain* 1984a;107:219-39.
- 5 Brown WF, Feasby TE. Sensory evoked potentials in Guillain-Barré polyneuropathy. *J Neurol Neurosurg Psychiatry* 1984;47:288-91.
- 6 Berger AR, Logigian EL, Shahani BT. Reversible proximal conduction block underlies rapid recovery in Guillain-Barré syndrome. *Muscle Nerve* 1988;11:1039-42.
- 7 Burkel WE. The histological fine structure of perineurium. *Anat Rec* 1967;158:177-90.
- 8 Olsson Y. Topographical differences in the vascular permeability of the peripheral nervous system. *Acta Neuropathol* 1968;10:26-33.
- 9 Jacobs JM, MacFarlane RM, Cavanaugh JB. Vascular leakage in the dorsal root ganglia of the rat, studied with horseradish peroxidase. *J Neurol Sci* 1976;29:95-107.
- 10 Seitz RJ, Heininger K, Schwendemann G, Toyka KV, Wechsler W. The mouse blood-brain barrier and blood-nerve barrier for IgG: A tracer study by use of the avidin-biotin system. *Acta Neuropathol (Berl)* 1985;68:15-21.
- 11 Asbury AK. Diagnostic considerations in Guillain-Barré syndrome. *Ann Neurol* 1981;9(suppl):1-5.
- 12 Hughes RAC, Kadlubarowski M, Hufschmidt A. Treatment of acute inflammatory polyneuropathy. *Ann Neurol* 1981;9(suppl):125-33.
- 13 Feasby TE, Gilbert JJ, Brown WF, *et al*. Acute axonal form of Guillain-Barré polyneuropathy. *Brain* 1986;109:1115-26.
- 14 Cornblath DR, Melts ED, Griffin JW, *et al* and the Guillain-Barré Study Group. Motor conduction studies in Guillain-Barré syndrome: description and prognostic value. *Ann Neurol* 1988;23:354-9.
- 15 Miller RG, Peterson GW, Daube JE, Albers JW. Prognostic value of electrodiagnosis in Guillain-Barré syndrome. *Muscle Nerve* 1988;11:769-74.
- 16 Yates SK, Hurst LN, Brown WF. The pathogenesis of pneumatic tourniquet paralysis in man. *J Neurol Neurosurg Psychiatry* 1981;44:759-67.
- 17 Dengler R, Stein RB, Thomas CK. Axonal conduction velocity and force of single human motor units. *Muscle Nerve* 1988;11:136-45.
- 18 Brown WF. *The physiological and technical basis of electromyography*. Boston: Butterworths, 1984.
- 19 Mills KR, Murray NMF. Proximal conduction block in early Guillain-Barré syndrome. *Lancet* 1985;ii:659.
- 20 Erlinger J, Schoepfle GM. A study of nerve degeneration and regeneration. *Am J Physiol* 1946;147:550-81.
- 21 Haymaker W, Kernohan JW. The Landry-Guillain-Barré syndrome. A clinicopathological report of fifty fatal cases and a critique of the literature. *Medicine (Baltimore)* 1949;28:59-141.
- 22 Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis. Its role in pathogenesis. *Medicine (Baltimore)* 1969;48:173-215.