

# Phrenic nerve stimulation in normal subjects and in patients with diaphragmatic weakness

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**ABSTRACT** Phrenic nerve stimulation is often considered to be difficult and unreliable. The time taken for the phrenic nerves to be located and adequately stimulated was measured in 110 subjects, aged 21-89 years, 26 of whom had diaphragmatic weakness; and phrenic nerve conduction time was recorded in 76 of these individuals. Each phrenic nerve was stimulated transcutaneously in the neck with square wave impulses 0.1 ms in duration at 1 Hz and 80-160 volts while diaphragmatic muscle action potentials were recorded with surface electrodes. The time taken to locate either phrenic nerve ranged from two seconds to 22 minutes (median 10 s). Both nerves were located in 83 of the 84 control subjects (99%) and in 21 of the 26 patients with diaphragmatic weakness (81%). Mean (SD) phrenic nerve conduction time in the control subjects was 6.94 (0.77) ms on the right and 6.61 (0.77) ms on the left. A weak relationship was found between conduction time and the subjects' age and height. Four out of 24 patients with diaphragmatic weakness had a prolonged phrenic nerve conduction time. Transcutaneous stimulation of the phrenic nerves was not a time consuming procedure, and it was well tolerated, reproducible, and successful in 95% of subjects.

Assessment of phrenic nerve function is necessary in candidates for permanent diaphragm pacing<sup>1</sup> and may be required in the investigation of patients with diaphragmatic weakness. Phrenic nerve conduction time provides a sensitive indicator of phrenic nerve function when the nerves are affected either by local lesions or by generalised neuropathies. Prolonged conduction time has been found in phrenic neuritis,<sup>2</sup> in mediastinal tumour, after surgical trauma,<sup>3</sup> and in peripheral neuropathies.<sup>4</sup>

Although percutaneous phrenic nerve stimulation was described in 1951<sup>5</sup> as a means of providing ventilatory support and again in 1967<sup>4</sup> as a method of investigation, phrenic nerve studies have not gained wide acceptance. Failure to locate the nerves,<sup>6,7</sup> and discomfort have been considered to be important problems. The purpose of this study was to establish how often, how quickly, and how reproducibly each phrenic nerve could be located by means of twitch stimulations, to see whether this investigation could be applied routinely. Studies were performed in control subjects to determine the normal range of phrenic nerve conduction time and in patients with

diaphragmatic weakness to establish (a) whether difficulty in locating the phrenic nerves was related to the degree of diaphragmatic weakness, and (b) whether phrenic neuropathy occurred commonly in patients with diaphragmatic dysfunction.

## Methods

We studied 110 subjects—84 healthy controls and 26 patients with diaphragmatic weakness. The control subjects, 36 women and 48 men, ranged in age from 21 to 89 years, with a mean of 42 years. Their height ranged from 152 to 205 (mean 172) cm. The patients' age ranged from 26 to 73 years with a mean of 49 years. Their height ranged from 157 to 200 (mean 170) cm. Diaphragmatic weakness was due to a variety of causes (table 1). All subjects gave informed consent for the studies.

Subjects were studied supine on a couch with a single pillow. The right and left phrenic nerves were stimulated at the posterior border of the sternomastoid muscle at the level of the cricoid cartilage.<sup>5</sup> Stimulation was performed with a pair of surface bipolar stimulating electrodes (Medelec 53054), with felt tips, 5 mm in diameter. Square wave impulses 0.1 ms in duration were delivered by a dual Digitimer 3072 isolated stimulator at a frequency of 1 Hz.

Diaphragm muscle action potentials were recorded

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Accepted 1 July 1987

Table 1 Clinical diagnoses in 26 patients with diaphragmatic weakness

Diagnosis	No
Myasthenia gravis	7
Connective tissue disorder	3
Polymyositis	2
Muscular dystrophy	2
Phrenic nerve injury	2
Multiple sclerosis	1
Poliomyelitis	1
Neuralgic amyotrophy	1
Idiopathic	7

with surface electrodes (Nikomed 460) placed in the seventh and eighth intercostal spaces, 2–3 cm from the costal margin on either side. The electromyogram (EMG) signals were processed with an amplifier (Medelec PA63) and were filtered below 80 Hz and above 1.6K Hz.

The stimulation voltage was increased until there was no further increase in the size of the diaphragm muscle action potential, and was then increased by a further 10%. The voltage required to achieve supra-maximal stimulation varied from 80 to 160 v. From 5 to 30 muscle action potentials were obtained and displayed on a Tektronix 5103N storage oscilloscope. The subjects breathed quietly throughout.

Oesophageal (Poes) and gastric (Pg) pressures were measured with balloon catheter systems<sup>8</sup> in 40 of the control subjects and in the patients with diaphragmatic weakness. Transdiaphragmatic pressure (Pdi), obtained electronically by subtracting Poes from Pg, was measured while subjects were seated during a series of sharp maximal sniffs (sniff Pdi) to provide a measure of diaphragmatic strength.<sup>9</sup>

The time taken to locate the phrenic nerves was measured in each of the 110 subjects. Timing was started when the operator moved the stimulating electrode towards the neck of the subject, and was stopped when the first definite diaphragm contraction was confirmed by EMG recordings. If the diaphragm muscle action potentials could not be obtained during phrenic nerve stimulation after 30 minutes, it was considered that the relevant stimulation could not be achieved. The times taken to locate first the right and then the left phrenic nerves were recorded separately.

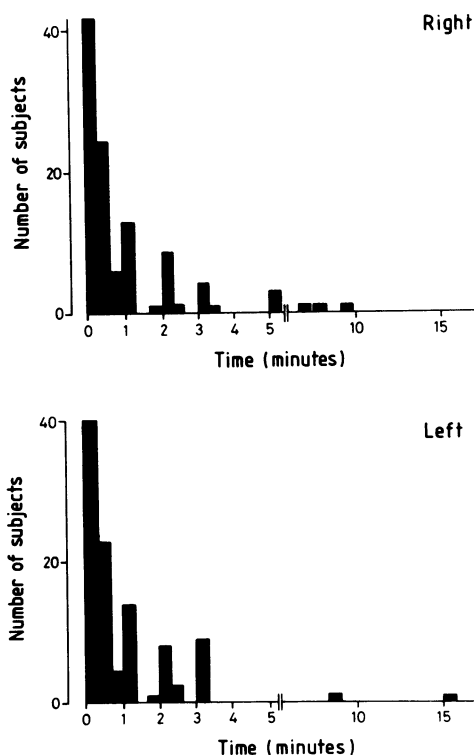
The conduction time of each phrenic nerve (terminal motor latency) was measured in 50 of the control subjects and in the 26 patients with diaphragmatic weakness, being taken as the time from the stimulus artefact to the onset of the diaphragm muscle action potential. Reproducibility of conduction time was measured in four control subjects on six separate days in the course of three to 12 months.

Group data were expressed as means with standard deviations in parentheses. The Wilcoxon signed rank

procedure test was used to compare times taken to locate the right and left phrenic nerves. Comparison of right and left conduction times were tested for statistical significance with the two tailed paired and unpaired Student's *t* tests as appropriate. Simple correlations were obtained by measuring the Kendall's rank and Pearson's correlation coefficients. For multiple linear regression analysis we used Minitab (a statistical package data analysis system, Pennsylvania State University, 1982) to investigate the relationship between phrenic nerve conduction time and subjects age and height.

## Results

Transdiaphragmatic pressure recorded during a maximal sniff in the 40 control subjects was 113.5 (23.1) cm H<sub>2</sub>O, ranging from 100 to 160 cm H<sub>2</sub>O in the men (normal > 98 cm H<sub>2</sub>O) and from 75 to 125 cm H<sub>2</sub>O in the women, (normal > 70 cm H<sub>2</sub>O).<sup>9</sup> Sniff Pdi in the patients with diaphragmatic weakness was 53.1 (30.1) cm H<sub>2</sub>O, ranging from 7 to 97 cm H<sub>2</sub>O in the men and from 15 to 68 cm H<sub>2</sub>O in the women. Phrenic nerve stimulation was well tolerated in all subjects but one, who had had surgery on the cervical



Times taken to locate right and left phrenic nerves.

spine and complained of severe hyperaesthesiae in the neck.

There was no significant difference between the times taken to locate the right and left nerves in the control subjects, in the patients, or in the group as a whole. The median time (figure) was 10 seconds and ranged from two seconds to 20 minutes. Both nerves were located in 83 of the 84 control subjects (99%) and in 21 of the 26 patients (81%). Diaphragmatic muscle action potentials could not be obtained on either side in two patients, both with very severe diaphragmatic weakness. One had acute myositis and was being treated with intermittent positive pressure ventilation and the other had muscular dystrophy. In four other subjects only one nerve could be located. One was a normal individual with a short obese neck and the other three were patients with diaphragmatic weakness. Of these, the first had sustained an injury to the phrenic nerve during surgery to the cervical spine, the second had polymyositis, and the third had in the past suffered from poliomyelitis.

The upper (99%) confidence limit for phrenic nerve conduction times in the control subjects was 9.25 ms for the right and 8.92 ms for the left. Mean conduction time was longer on the right than the left (table 2). This difference was significant ( $p < 0.001$ ), but was never more than 1.0 ms. Measurement of phrenic nerve conduction time was highly reproducible from day to day in the four subjects tested; the mean (SD) coefficient of variation was 4.6% (1.9%) (range 3–9%). In the 50 control subjects multiple regression analysis showed a weak relationship of conduction time with age and height, as shown by the equation:

$$\text{Phrenic nerve conduction time} = 0.052 + 0.0159 \text{ age (y)} + 0.0326 \text{ height (cm)} \quad (r^2 = 26.5\%; p < 0.01).$$

There was no relation between phrenic nerve conduction times and the sex of the subjects.

Overall conduction times in patients with diaphragmatic weakness did not differ significantly from those in the control group ( $p = 0.09$ ), and the

mean conduction time in patients was not significantly longer on the right than on the left (table 2). Of the 24 patients with diaphragmatic weakness in whom unilateral or bilateral phrenic nerve conduction times could be recorded, 20 had values in the normal range. Conduction time was, however, prolonged in four patients: one was thought to have neuralgic amyotrophy (conduction times: right 5.6 ms, left 14.6 ms); another had poliomyelitis (right not obtained, left 12.0 ms); and the other two had a history of trauma to the affected phrenic nerve, caused respectively by complications of surgery to the cervical spine (right 13.0 ms, left not obtained) and by a therapeutic phrenic nerve crush for pulmonary tuberculosis 29 years previously (right 16.0 ms, left 7.5 ms).

There was no relationship between the time taken to locate either the right or the left phrenic nerve and diaphragmatic strength in those patients in whom stimulation was successful. Furthermore, there was no correlation between conduction time and the height of sniff Pdi in either the control subjects or the patients.

## Discussion

These studies show that percutaneous phrenic nerve stimulation is an easy and rapid procedure that achieves successful stimulation of the phrenic nerves. It was associated with little or no discomfort. The phrenic nerves were located in 95% of the 110 cases studied within a median time of 10 seconds. Stimulation was successful on both sides in all but one control subject and five patients with diaphragmatic weakness.

Stimulation did not prove to be more difficult in patients who were appreciably dyspnoeic at rest, but was less easy in those with short or obese necks. The phrenic nerves could not be located in all cases; possibly an abnormal position of the phrenic nerves was a cause of failure.<sup>10</sup>

Various techniques for stimulating the phrenic nerves have previously been reported. Originally a thimble electrode applied over the operator's forefinger was used.<sup>5</sup> Needle electrodes, inserted in the vicinity of the nerve, have been used in an attempt to ensure better stimulation and to reduce patients' discomfort.<sup>11 12</sup> Similarly, methods of recording the diaphragm muscle action potential have varied. Needle electrodes have been inserted through the chest wall<sup>13</sup> and oesophageal electrodes<sup>14 15</sup> have been used. We found, however, that percutaneous stimulation, by means of a conventional bipolar stimulating electrode with recording of the diaphragm action potential from surface electrodes, was not only non-invasive but also appeared to be easy, quick, and successful.

Table 2 Phrenic nerve conduction times (milliseconds)

	Right	Left	Right-left difference
<b>NORMAL SUBJECTS</b>			
No	50	50	50
Mean	6.94	6.61	0.33 ( $p < 0.001$ )
SD	0.77	0.77	0.48
Range	6.0–9.0	5.5–8.0	0–1.0
<b>PATIENTS</b>			
No	22	23	20
Mean	7.70	7.30	0.40 (NS)
SD	2.51	1.34	1.95
Range	4.5–16.0	5.0–12.0	0–8.5

In one previous study, conduction time of the left phrenic nerve was found to be slightly longer than that of the right<sup>14</sup> and this was thought to be because the left phrenic nerve is longer than the right. Other workers found no significant difference between the two sides<sup>11 15 16</sup> or a longer conduction time on the right.<sup>3</sup> The last finding is in agreement with our results. Significant correlation between right and left phrenic nerve conduction time ( $r = 0.81$ ,  $p < 0.001$ ) was found in the 50 control subjects studied, indicating that if one side deviated from the mean value the other side tended also to deviate in the same direction.

Since the conduction velocity of motor fibres decreases with age<sup>17</sup> phrenic nerve conduction time would be expected to increase with age. Similarly, conduction time would be expected to increase with the length of the nerve, and hence with the height of the subject. Our data showed a weak relationship between phrenic nerve conduction and subjects' age and height. In one previous study<sup>11</sup> a weak correlation was found only with age and no correlation was found with height, while other studies found no relationship with either.<sup>4 16</sup> The reason may be that the range of both the age (21–89 years) and the height (152–205 cm) of control subjects in our study was wider than that of the groups previously investigated. More recently, however, a positive correlation has also been found between phrenic nerve conduction time and both age and height in a group of subjects whose age range was only 21–66 years and height range 163–190 cm.<sup>15</sup> These workers found that phrenic nerve conduction times were on average 1 ms shorter when oesophageal electrodes were used than when surface electrodes were placed at different sites on the chest wall, but this finding would be unlikely to have affected the relationship they found between age and height. As anticipated, we found no significant difference in conduction time between men and women when differences in height had been accounted for.

Although no relationship was found between the time taken to locate the phrenic nerves and diaphragmatic strength, the observation that location was unsuccessful in two patients with severe diaphragmatic weakness suggests that the test might be more difficult to apply in patients with severe weakness. Nevertheless, phrenic neuropathy was found in four of the 26 weak patients, suggesting that phrenic nerve studies are important in the investigation of patients with diaphragmatic weakness. The finding of a very slightly prolonged conduction time in the patient who had had poliomyelitis is consistent with reports of mildly reduced conduction velocities in peripheral limb nerves in such patients, when the fastest conducting fibres are lost.

Location of the phrenic nerves and measurement of conduction time are not only reliable but rapid and

simple to perform. Phrenic nerve studies are useful in the clinical investigation of breathless patients, especially those with suspected local lesions of the phrenic nerves.

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