# Phrenic nerve conduction in man[1]

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In 1936, Heinbecker, Bishop, and O'Leary measured phrenic nerve conduction velocity in human specimens obtained at operation or from cadavers, quoting a figure of 78 m./sec. No further studies in man appear to have been made since that time; in particular no information is available on phrenic nerve conduction *in vivo*.

Impairment of phrenic nerve conduction is usually inferred from reduced or paradoxical diaphragmatic movement seen on x-ray screening but interpretation is not always easy, especially when both halves of the diaphragm are involved. The present work arose from just such a diagnostic difficulty, when it became apparent that a more direct assessment of phrenic nerve function was needed.

Previous attempts to record the electrical activity of the diaphragm have required either the use of oesophageal electrodes, or of needle electrodes inserted through the chest wall to avoid interference from the intercostal muscles (Taylor, 1960). However, in the present work, it has been found that the electrical activity in the diaphragm can be readily recorded from surface electrodes over the lower intercostal spaces when a twitch is evoked in the muscle by phrenic nerve stimulation in the neck.

With this technique, phrenic nerve conduction time has been measured in a group of control subjects. Further studies in patients with neurological disorder have shown that phrenic nerve conduction time is a sensitive index of involvement of the nerve by disease both in local lesions of the phrenic nerve and in generalized neuropathy.

### MATERIALS AND METHOD

Measurements were made on 18 control subjects. Nine patients with peripheral neuropathy and eight patients with suspected local lesions of the phrenic nerve were also studied. Subjects were examined in a warm room lying supine on a couch with the head slightly raised. Breath-holding during recording was not found to be necessary in the majority of cases.

The phrenic nerve can be stimulated percutaneously in healthy subjects at the posterior border of the sternomastoid muscle at the level of the upper margin of the thyroid cartilage (Whittenberger, Sarnoff, and Hardenbergh, 1949). A brief search was sometimes required before the nerve was located. Because the phrenic nerve at this point lies in close relation to the brachial plexus, stimulation sometimes caused excitation of upper limb muscles. However, with careful placing of the stimulating electrode selective excitation of the phrenic nerve could usually be achieved. An isolated stimulator (Morton, 1965; Devices Sales Ltd.) delivered pulses of 0·2 to 1·0 msec. duration at a repetition rate of 1/sec.; the cathode was a circular saline pad of 1 cm. diameter and the anode was a metal plate (3·5 cm. × 6 cm.) strapped over the manubrium sterni.

The diaphragmatic muscle action potential was recorded with either silver cup or suction cup electrodes placed 3·5 cm. to 5 cm. apart in the eighth, or eighth and ninth interspaces, with the anterior electrode in the anterior axillary line (Fig. 2). Preliminary experiments indicated that the most satisfactory recordings could be obtained from the seventh, eighth, or ninth interspaces on the antero-lateral aspect of the chest wall, the
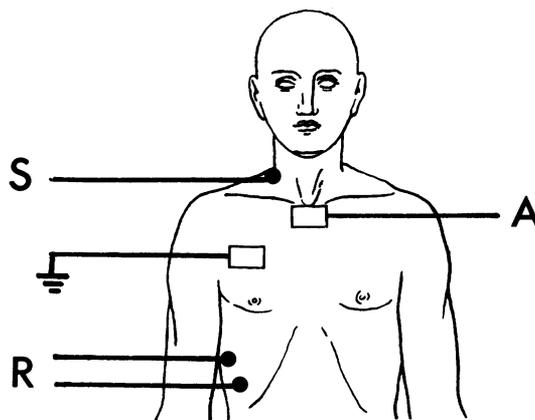


FIG. 1. *Arrangement of stimulating electrode (S), anode (A), and recording electrodes (R) used for determining phrenic nerve conduction time. The nerve is stimulated behind the posterior border of the sternomastoid muscle at the level of the thyroid cartilage, and the recording electrodes are in the eighth intercostal space (see Fig. 2).*
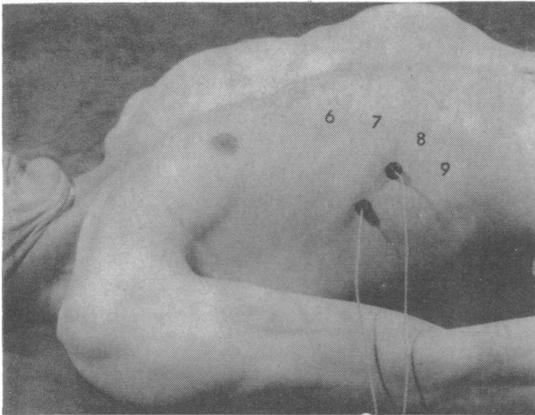
FIG. 2. *Recording electrodes in the eighth intercostal space.*



FIG. 3. *Control subject. Action potential recorded with surface electrodes in the eighth intercostal space on phrenic nerve stimulation in the neck. Five traces superimposed.*

amplitude of the response progressively diminishing above or below these spaces. An earth plate (3·5 cm. × 6 cm.) was applied over the upper chest wall.

The muscle action potential was displayed on one beam of the Stanley Cox double electromyograph with a time scale on the second beam. The latency of the mechanical response of the chest wall caused by the diaphragmatic twitch was also measured in some subjects. For this a small crystal microphone functioning as a mechano-electrical transducer was strapped to the chest wall close to the recording electrodes. The response was displayed on the second beam of the electromyograph. In two subjects undergoing thoracotomy, plaited stainless steel electrodes were sewn into the diaphragm under direct vision and brought out through the chest wall. Recordings were then made during the first post-operative week, after which the electrodes were gently withdrawn.

### RESULTS

NATURE OF THE RESPONSE RECORDED WITH SURFACE ELECTRODES    In Fig. 3 is shown a typical response recorded with surface electrodes over the eighth intercostal space, on phrenic nerve stimulation in the neck, five traces being superimposed. The latency to the onset of electrical activity is 8 msec. in this subject, and the duration of the response slightly less than 40 msec. In order to establish that this response represents the compound diaphragmatic muscle action potential and is not a consequence of movement artefact, two separate groups of observations were made.

First, the latency of the mechanical response of the chest wall to the diaphragmatic twitch was measured and compared with the latency of the electrical response, as shown in Fig. 4 for a healthy
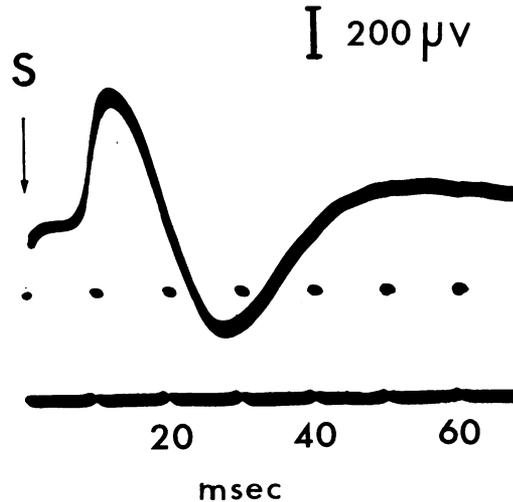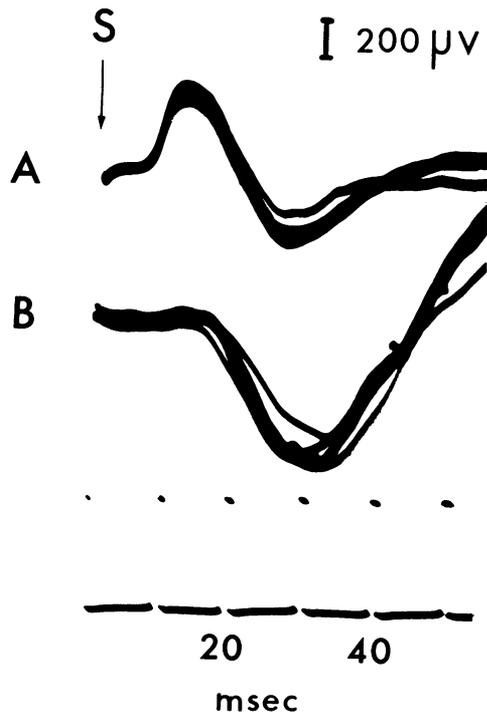


FIG. 4. *Control subject. Simultaneous recording of action potential with surface electrodes (A) and mechanical effect of diaphragmatic twitch with transducer (B) following phrenic nerve stimulation. The electrical response recorded with surface electrodes precedes the mechanical effects of the diaphragmatic twitch by 6·6 msec. Five traces superimposed.*

subject. It can be seen that the onset of electrical activity recorded with surface electrodes (upper trace) precedes the mechanical response (lower trace) by about 6 msec. A comparable delay of the mechanical response compared with the electrical response was demonstrated in the 21 subjects in whom it was measured, as shown in Figure 5. It follows that the initial deflection on the tracing obtained with surface electrodes is not due to movement artefact.
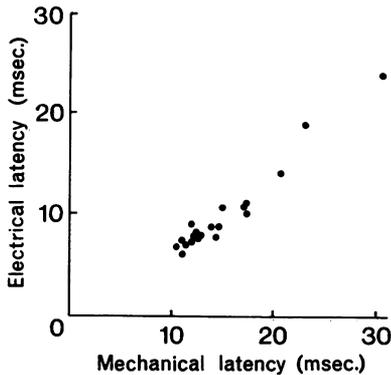


FIG. 5. *The latency of the electrical response recorded with surface electrodes plotted against the latency of the mechanical effects of the diaphragmatic twitch for 21 subjects. In all cases the electrical response preceded the mechanical response.*

A second experimental observation confirmed that the tracing from surface electrodes represented the true diaphragmatic muscle action potential. This was obtained by direct recording from paired wire electrodes sewn into the diaphragm in two subjects undergoing thoracotomy. The records from one of these subjects is shown in Figure 6. The response from the indwelling diaphragmatic electrodes is on the upper trace and the response recorded with surface electrodes on the lower trace. The onset of activity is almost synchronous for the two recording sites.

These observations establish that the diaphragmatic compound muscle action potential can be recorded with surface electrodes over the lower chest wall on ipsilateral phrenic nerve stimulation in the neck.

PHRENIC NERVE CONDUCTION TIME IN CONTROL SUBJECTS Phrenic nerve conduction time is used here to indicate the time interval between stimulation of the phrenic nerve in the neck and the onset of the diaphragmatic muscle action potential recorded over the lower chest wall. It was measured in 18 control

subjects, bilaterally in four of them. Some of these subjects were healthy medical workers and the others patients without evidence of pathology in the peripheral nerves or upper cervical cord. Their ages ranged from 20 to 61. The values for conduction time lay between 6·1 and 9·2 msec., mean 7·7 (S.D. ± 0·80) msec., and are indicated as a histogram in Figure 7. No correlation of conduction time with age was present.

The amplitude of the diaphragmatic muscle action potential in these subjects varied from 160 to 500μv., and there was poor correlation between amplitude and conduction time.

PHRENIC NERVE CONDUCTION TIME IN PERIPHERAL NEUROPATHY There were nine patients in this group; the diagnosis for each individual is given in Table I. Forearm conduction velocity in either median or ulnar nerve was recorded in every subject, and vital capacity was measured in six.

The values for phrenic nerve conduction time have been compared with those of the control subjects in
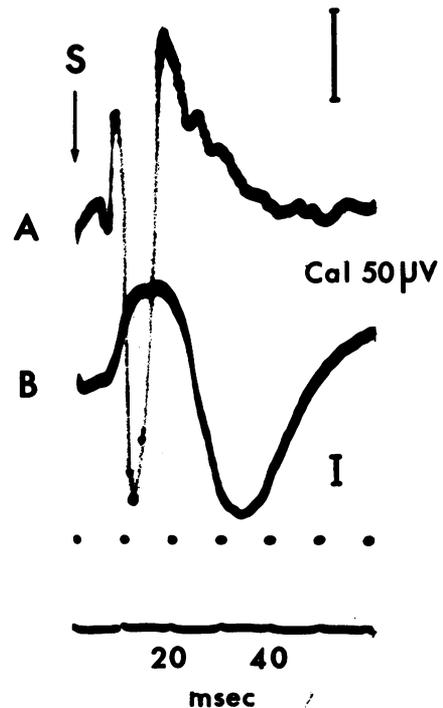


FIG. 6. *Control subject. Simultaneous recording of action potential with indwelling diaphragmatic electrodes (A, tracing retouched) and compound muscle action potential with surface electrodes (B) on phrenic nerve stimulation. The onset of the action potential is virtually synchronous from the two recording sites.*

## TABLE I

### NINE PATIENTS WITH PERIPHERAL NEUROPATHY

| Subject | Age | Diagnosis | Duration | Phrenic Nerve Conduction Time (msec.) | Forearm Conduction Velocity (m./sec.) | Vital Capacity (% predicted) |
|---------|-----|-----------|----------|----------------|-----------|----------------|
| E.H. | 55 | Scleroderma | 6 years | 33·3 | 16 | — |
| J.Sa. | 41 | Déjerine-Sottas | 15 years | 23·7 | 12 | 125 |
| H.D. | 39 | Déjerine-Sottas | 4 years | 19·0 | 33 | 107 |
| L.M. | 66 | Unknown | 2 years | 17·3 | 19 | 93 |
| A.P. | 55 | Carcinomatous neuropathy (bronchus) | 10 months | 14·1 11·6 | 43 | — |
| M.B. | 71 | Guillain-Barré | 1 month | 11·2 | 36 | — |
| J.M. | 50 | Unknown | 8 years | 10·1 | 38 | 87 |
| A.L. | 30 | Polyarteritis | 4 months | 7·3 | 60 | 82 |
| J.S. | 62 | Unknown | 1½ years | Inexcitable | Inexcitable | 44 |
| Normal Values | | | | 6·1–9·2 | 48–68 | |
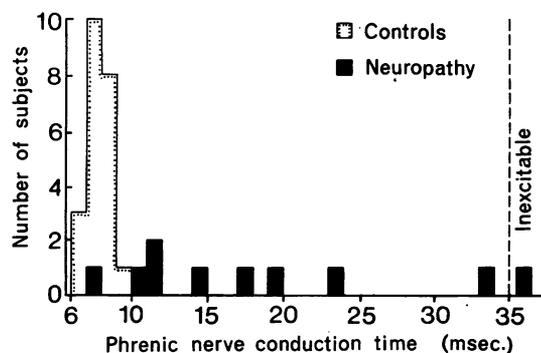


FIG. 7. *Histogram comparing phrenic nerve conduction time between control subjects and patients with peripheral neuropathy.*

a histogram (Fig. 7). In only one case (A.L.) was the conduction time within the range of the controls. The most marked slowing of conduction was in a patient with scleroderma in whom the conduction time was 33·3 msec. Considerable impairment of conduction was present in the two patients with Déjerine-Sottas disease, and the record obtained in one of them is shown in Fig. 8, in which five traces have been superimposed. Conduction time in this case was 23·7 msec. In the patient (A.P.) with neuropathy secondary to bronchial carcinoma, conduction time was measured in both phrenic nerves; greater slowing of conduction was present on the side of the primary growth, where the chest radiograph showed a mass at the hilum of the lung, thus raising the possibility of local involvement of the nerve by tumour. In one subject (J.S.) the phrenic nerve could not be excited with the maximum stimulus tolerated.

Forearm conduction velocity in these patients was directly related to phrenic nerve conduction time, as


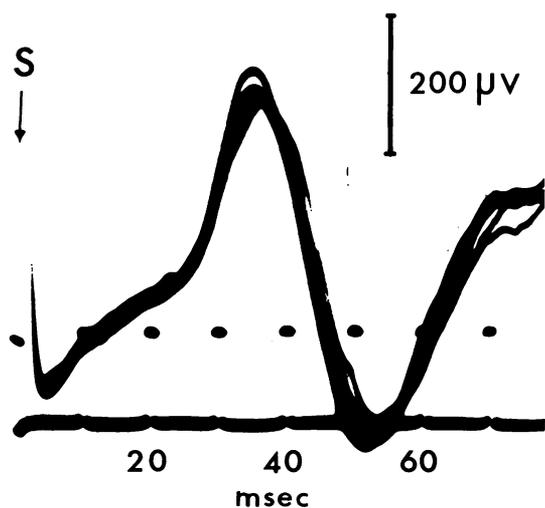
FIG. 8. *Patient with Déjerine-Sottas disease (J. Sa.). Prolongation of phrenic nerve conduction time (23·7 msec.). Five traces superimposed.*
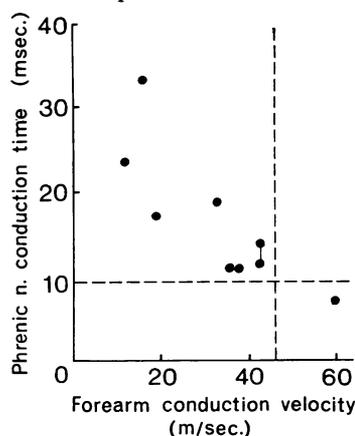


FIG. 9. *Phrenic nerve conduction time plotted against forearm conduction velocity in eight patients with peripheral neuropathy. The limits of the normal range are indicated by broken lines.*

indicated in Figure 9. The limits of the range of the two measurements in healthy subjects are indicated. The only patient (A.L.) whose phrenic nerve conduction time was within the range of the control subjects had a normal forearm conduction velocity. The two subjects with greatest slowing of conduction velocity in the forearm also had the greatest prolongation of conduction time in the phrenic nerve. In the patient (J.S.) whose phrenic nerve was inexcitable, the median and ulnar nerves were also inexcitable.

The vital capacity was expressed as a percentage of that predicted from height, age, and sex (Table I). In only one patient (J.S.) was it significantly reduced. The two patients with Déjerine-Sottas disease, in whom phrenic nerve conduction was markedly impaired, had values for their vital capacities which did not fall below that predicted; indeed in subject J.Sa. the measured value exceeded the predicted value by 25%.

In the patient with scleroderma (E.H.), who had the greatest impairment of phrenic nerve conduction, necropsy material became available. When single fibres from the phrenic nerve were stained with 1% osmium tetroxide (Thomas, 1955), widespread segmental demyelination was seen and similar changes were found in the limb nerves.

PHRENIC NERVE CONDUCTION TIME IN LOCAL LESIONS OF THE PHRENIC NERVE Phrenic nerve conduction was studied bilaterally in four patients in whom the nerve was at risk from a bronchial carcinoma, in two patients with suspected surgical damage to the nerve, and in two patients with isolated diaphragmatic paralysis of unknown cause (Table II).

The four patients with bronchial carcinoma had x-ray evidence of lesions close to the hilum of the lung. The integrity of the phrenic nerve was established, however, since conduction time on the side of the tumour was within the range of the control subjects in all cases. In one subject, conduction time in the contralateral nerve was just outside the control range.

The two patients with suspected surgical damage to the phrenic nerve had recently undergone

pericardectomy for chronic pericarditis. The nerve had not been identified at operation because of pericardial thickening, and it was uncertain whether it had been damaged. It was not possible to assess the extent of diaphragmatic paralysis on the chest radiograph because of post-operative pleural effusion and lung collapse, and electrical studies were requested.

In both cases, the phrenic nerve proved to be inexcitable on the side of the pericardectomy, while the contralateral conduction time was within or close to the control range. In one of these subjects (E.D.), the phrenic nerve remained inexcitable six months later.

Of the two patients with isolated unilateral diaphragmatic paralysis, symptoms had been present for one month in one and three years in the other. The chest radiograph was normal in both cases apart from the raised hemidiaphragm. The phrenic nerve was inexcitable in both subjects on the side of the diaphragmatic paralysis, whereas conduction time was within the control range on the contralateral side.

DISCUSSION

The electrical activity of the diaphragm cannot normally be distinguished from that of the intercostal muscles when recording with surface electrodes over the chest wall (Campbell, 1958). In these experiments, however, it has proved possible to record with surface electrodes the diaphragmatic muscle action potential associated with an electrically evoked diaphragmatic twitch, so that phrenic nerve conduction can be measured. For the clinical application of this technique, recording with surface electrodes is more comfortable for the subject than the use of oesophageal electrodes or sampling with needle electrodes inserted through the lower chest wall.

Possible sources of error in this type of recording must be considered. First, artefact from movement of the chest wall due to the diaphragmatic twitch itself has been excluded by measuring the onset of the mechanical event and showing that it is preceded

TABLE II

PHRENIC NERVE CONDUCTION TIME IN LOCAL LESIONS OF PHRENIC NERVE

| Subject | Age | Diagnosis | Phrenic Nerve Conduction Time (msec.) | |
|---|---|---|---|---|
| | | | Right | Left |
| R.K. | 56 | Carcinoma left main bronchus | 9·9 | 9·1 |
| W.F. | 64 | Carcinoma right upper lobe bronchus | 8·9 | 9·1 |
| W.H. | 59 | Carcinoma left lower lobe bronchus | 8·2 | 8·3 |
| H.K. | 74 | Carcinoma bronchus: left hilar mass | 8·3 | 8·8 |
| E.B. | 46 | Left pericardectomy for chronic constrictive pericarditis | 8·2 | Inexcitable |
| E.D. | 54 | Left pericardectomy for chronic constrictive pericarditis | 9·5 | Inexcitable |
| W.G. | 71 | Idiopathic left diaphragm paralysis | 8·2 | Inexcitable |
| | 53 | Idiopathic left diaphragm paralysis | 7·9 | Inexcitable |

by the electrical response recorded with surface electrodes. Movement artefact may also result from activation of other muscle groups by the stimulus. In healthy subjects, it was usually possible to limit excitation to the phrenic nerve alone by careful placing of the stimulating electrode; when the electrode was moved away from the phrenic nerve to cause excitation of the pectoral and arm muscles, the characteristic diaphragmatic potential was replaced by an irregular potential of longer latency. Where higher stimulus intensities were employed, as in isolated phrenic nerve lesions, associated excitation of the brachial plexus could not always be avoided, but the presence of a visible diaphragmatic twitch and the latency of the mechanical events recorded with the transducer helped to determine the nature of the recorded potential.

Previous accounts of phrenic nerve stimulation in man relate to its use in artificial ventilation (Whittenberger *et al.*, 1949; Sarnoff, Maloney, Sarnoff, Ferris, and Whittenberger, 1950). In this technique, a rhythmic tetanizing stimulus (40/sec.) of varying voltage is directed to one phrenic nerve. Since the vagus nerve lies fairly close to the phrenic nerve at its site of stimulation in the neck, these authors looked for the effects of vagal stimulation. In 100 cases of acute bulbar poliomyelitis no bradycardia occurred during the phase of phrenic stimulation. No vagal effects have been apparent in the present study.

In the intact subject it is not possible to measure conduction velocity in the phrenic nerve. However, in the patients with peripheral neuropathy, conduction time in the phrenic nerve correlated well with conduction velocity in a forearm nerve so that conduction time clearly provides a reliable assessment of phrenic nerve function.

The amplitude of the diaphragmatic action potential, on the other hand, was a less reliable guide to phrenic nerve function, showing a variable relationship with conduction time. This is likely to be accounted for by the variable depth of lung tissue which separates the recording electrodes from the diaphragm.

Ventilatory failure is a well-known complication of peripheral neuropathy so that an early indication of involvement of the nerves to the respiratory muscles is desirable. Fluoroscopic examination of the diaphragm would be of little value since both halves of the muscle will be affected. A reduction in vital capacity might be expected early in the disease process, but the findings in the present study do not support this. The vital capacity was within the predicted range in five out of six subjects with peripheral neuropathy while all of them show prolongation of phrenic nerve conduction time; in

the remaining subject, vital capacity was severely reduced and the phrenic nerve inexcitable. Phrenic nerve conduction time therefore provides the earliest indication that the disease process is involving the innervation of the respiratory muscles, and that ventilatory insufficiency may be a future complication.

The histological changes of segmental demyelination in the phrenic nerve of the patient (E.H.) with scleroderma are of interest in relation to the observed severe impairment of conduction in the nerve since markedly reduced conduction velocity is known to be associated with segmental demyelination (for references, see Gilliatt, 1966).

Isolated lesions of the phrenic nerve are usually investigated by diaphragmatic screening, but interpretation is not always easy (Simon, 1962). The presence of a pleural effusion or of a collapsed lung, for instance, may make it difficult to visualize the extent of diaphragmatic movement. Furthermore, although paradoxical movement of the diaphragm on sniffing has in the past been widely accepted as a sign of paralysis, recently Alexander (1966) has reported this finding in 6% of normal subjects. Direct measurement of phrenic nerve conduction time in these cases should provide an additional diagnostic procedure.

### SUMMARY

The diaphragmatic compound muscle action potential has been recorded with surface electrodes over the lateral chest wall when a twitch is evoked in the muscle by phrenic nerve stimulation in the neck. This has been confirmed by simultaneous recording from indwelling diaphragmatic electrodes.

The mean value for conduction time in the phrenic nerve of healthy subjects was 7·7 (S.D. ± 0·80) msec. Prolongation of conduction time was demonstrated in eight out of nine patients with peripheral neuropathy. Eight patients with isolated phrenic nerve lesions were also studied. The clinical application of this technique is discussed.

### ADDENDUM

A study by Delhez (1965) has recently come to notice in which the action potential from crural fibres of the diaphragm was recorded with an oesophageal electrode in healthy subjects, after phrenic nerve stimulation. The values for phrenic nerve conduction time accord well with those obtained in the present work.

O'Sullivan for the histological study on patient E.H. I would like to thank Dr. Pamela Fullerton for helpful advice and Professor Gilliatt for reading the draft of this paper.

## REFERENCES

Alexander, C. (1966). Diaphragm movements and the diagnosis of diaphragmatic paralysis. *Clin. Radiol.*, 17, 79-83.
Campbell, E. J. M. (1958). *The Respiratory Muscles*, p. 12. Lloyd-Luke, London.
Delhez, L. (1965). Modalités chez l'homme normal de la réponse électrique des piliers du diaphragme à la stimulation électrique des nerfs phréniques par des chocs uniques. *Arch. int. Physiol.*, 72, 832-839.
Gilliatt, R. W. (1966). Applied electrophysiology in nerve and muscle disease. *Proc. roy. Soc. Med.*, 59, 989-993.
Heinbecker, P., Bishop, G. H., and O'Leary, J. L. (1936). Functional and histologic studies of somatic and autonomic nerves of man. *Arch. Neurol. Psychiat. (Chic.)*, 35, 1233-1255.
Morton, H. B. (1965). A generator of isolated rectangular voltage pulses. *J. Physiol. (Lond.)*, 178, 31-32P.
Sarnoff, S. J., Maloney, J. V., Sarnoff, L. C., Ferris, B. G., and Whittenberger, J. L. (1950). Electrophrenic respiration in acute bulbar poliomyelitis. *J. Amer. med. Ass.*, 143, 1383-1390.
Simon, G. (1962). *Principles of Chest X-ray Diagnosis*, 2nd ed. Butterworths, London.
Taylor, A. (1960). The contribution of the intercostal muscles to the effort of respiration in man. *J. Physiol. (Lond.)*, 151, 390-402.
Thomas, P. K. (1955). Growth changes in the myelin sheath of peripheral nerve fibres in fishes. *Proc. roy. Soc. B*, 143, 380-391.
Whittenberger, J. L., Sarnoff, S. J., and Hardenbergh, E. (1949). Electrophrenic respiration. II. Its use in man. *J. clin. Invest.*, 28, 124-128.