Electrical stimulation to restore respiration

Graham Creasey, MD; John Elefteriades, MD; Anthony DiMarco, MD; Pasi Talonen, PhD; Manfred Bijak, MSc; Werner Girsch, MD; Carole Kantor, MS
MetroHealth Medical Center, Departments of Medicine and of Physical Medicine and Rehabilitation, Cleveland, OH 44109; Case Western Reserve University, Cleveland, OH 44106 Yale University School of Medicine, Department of Cardiothoracic Surgery, New Haven, CT 06520; Atrotech OY, Tampere, Finland SF33721; University of Vienna, Departments of Plastic Surgery and of Biomedical Engineering and Physics, Vienna, Austria A-1090; Tantalus, Inc., Highland Park, NJ 08904

Abstract—Electrical stimulation has been used for over 25 years to restore breathing to patients with high quadriplegia causing respiratory paralysis and patients with central alveolar hypoventilation. Three groups have developed electrical pacing systems for long-term support of respiration in humans. These systems consist of electrodes implanted on the phrenic nerves, connected by leads to a stimulator implanted under the skin, and powered and controlled from a battery-powered transmitter outside the body. The systems differ principally in the electrode design and stimulation waveform. Approximately 1,000 people worldwide have received one of the three phrenic pacing devices, most with strongly positive results: reduced risk of tracheal problems and chronic infection, the ability to speak and smell more normally, reduced risk of accidental interruption of respiration, greater independence, and reduced costs and time for ventilatory care. For patients with partial lesions of the phrenic nerves, intercostal muscle stimulation may supplement respiration.

Key words: central alveolar hypoventilation, diaphragm pacing, FES, phrenic nerve stimulation, respiratory paralysis.

INTRODUCTION

Electrical stimulation of the phrenic nerve to restore respiration was first suggested in 1783 by Hufeland (1) and then demonstrated as a method of cardiopulmonary resuscitation by Ure in 1819 (2), Duchenne de Boulogne in 1872 (3), and Beard and Rockwell in 1878 (4). In the early part of this century, transcutaneous phrenic nerve stimulation was tested in the acute treatment of apneic newborns by Israel and of polio patients by Sarnoff (5). Based on research starting in 1959, Glenn and colleagues developed chronic phrenic nerve stimulation (6–10). In this life-sustaining application of electrical stimulation, patients can breathe entirely by diaphragm pacing. Several groups that use Glenn’s method have demonstrated its effectiveness and clinical utility for long-term ventilation in patients with high quadriplegia or central hypoventilation. Investigators in Finland and Austria have developed variant electrodes and stimulation techniques in an attempt to reduce muscle fatigue and produce smoother contraction.

To expand the patient group who can be helped to breathe with electrical stimulation, other workers are studying intercostal muscle stimulation in patients with partial lesions of motor neurons supplying the diaphragm.
This paper reviews the current status of chronic implants for respiratory assist in humans by phrenic nerve stimulation to produce diaphragm contraction, and by extradural spinal cord stimulation to produce intercostal muscle contraction. It represents what the authors hope is a dialogue between clinicians and engineers in the service of improving electrical stimulation devices that will build on both commercial and research advances.

Phrenic Nerve Stimulation

Respiration is controlled principally by the medullary respiratory control center with some voluntary cerebral influence. The upper motor neurons of the system originate in cell bodies in the medullary respiratory control center. The axons of these neurons have synapses in the spinal cord in the neck at the levels C3 to C5, where they communicate with the lower motor neurons. The axons of the latter neurons form the phrenic nerves that innervate the diaphragm. Diaphragm pacing cannot treat primary neuromuscular disorder, primary phrenic nerve injury, or spinal cord injury (SCI) at levels C3 to C5. It can only treat conditions that affect the upper motor neurons or the medullary respiratory control center.

The two main indications are central alveolar hypoventilation (CAH, or Ondine’s curse) and high quadriplegia. In CAH, the brain fails to tell the body to breathe; this can occur when there is dysfunction in the chemoreceptors in the medulla or in the cortical influence on the medulla. CAH may follow stroke or encephalitis, it may be congenital, and in many cases it is idiopathic. High quadriplegia can result from tumor or encephalitis affecting the brain stem, or from spinal cord trauma at the C1–C2 level, which may be caused by motor vehicle accidents, gunshot wounds, falls, or diving injuries. In addition, defects may result from surgical trauma.

Evaluation of Candidates for Phrenic Pacing

In people with normal ventilatory control, an increase in arterial CO₂ (PaCO₂) produces an increase in ventilation, which prevents a decrease of PaO₂. Although hypoxemia does not cause an increase of ventilation in normal people (11), O₂ saturation is taken as the measure of ventilation because it is easier to monitor than PaCO₂. In people with CAH, there is almost no ventilatory response to hypercarbia.

When a person appears to have CAH, a 24-hour profile of heart rate, CO₂ level, O₂ saturation, and respiratory rate is performed in a sleep laboratory. In cases suspicious of acquired (adult) CAH, a full sleep study should be performed to exclude with certainty the possibility of obstructive sleep apnea.

The following additional procedures should precede any attempt to implant a stimulating device (10,12). The conduction of the phrenic nerve should be evaluated by transcutaneous stimulation with a thimble or needle electrode in the neck, using an indifferent surface electrode (anode) on the manubrium sterni. The trigger point lies against the scalene muscle lateral to the clavicular head of the sternocleidomastoid muscle at the level of the cricoid cartilage (13). Surface electrodes are used to record responses from the diaphragm; the active one is placed in the eighth intercostal space on the anterior axillary line, the reference electrode on the xiphoid, and the ground halfway between xiphoid and manubrium.

In adults (age range 18–74 years), mean onset latency is 7.5 ms (SD 0.6 ms) with an upper limit of 9.0 ms (13). In children, latencies are different; they decrease from birth (mean 2.6 ms, SD 0.3) to about 6 months of age (2.2 ms, SD 2.2) because of maturation of the nerve, and then increase (4.2 ms between 5 and 11 years) because of growing length (12,14).

The function of the diaphragm muscle should be tested using standard conditions under fluoroscopy (15). At supramaximal tetanic stimulation of the nerve, the diaphragm should descend at least 4 cm in adults. The descent should be recorded independently for each side to provide baseline values for possible future troubleshooting. The test is most easily performed in connection with measurement of phrenic nerve latency.

Additional requirements for receiving the phrenic pacing system are normal pulmonary function and normal chest wall configuration. The diaphragm must be intrinsically intact except for disuse atrophy in the case of quadriplegia. Good psychosocial conditions are important and a diaphragm pacer is not usually implanted in persons with significant cognitive injury. A supportive home situation is essential.

Implant Procedure

Three groups, located in the United States, Austria, and Finland, have developed pacing systems for long-term support of respiration in humans. These systems consist of electrodes implanted on the phrenic nerves and connected by leads to a stimulator implanted subcutaneously and powered and controlled by electromagnetic coupling from a battery-powered transmitter.
outside the body. The systems differ principally in the electrode design and stimulation waveform. The implant procedures also vary according to the devices and the surgeons carrying out the implantations.

Yale Group

The implantation procedure used by this group is a relatively noninvasive thoracic operation. A minithoracotomy, 3 to 4 in (7.6 to 10 cm) long, is made in the second or third intercostal space on the anterior chest wall. The phrenic nerve isatraumatically mobilized above a flat spot of the mediastinum at the top of the cardiac structures. The half-cuff electrode is placed behind the nerve, and the silastic portions of the electrode are secured to the pleura overlying the mediastinum. The nerve must lie perfectly inside the half-cuff platinum contact of the electrode with no distortion or tension. The full cuff used previously has potential for circumferential scar which may impair the nerve. With the 180°, or half-cuff, electrode, if scar develops, it is limited to one side and cannot trap or pinch the nerve.

Through a smaller incision (2 in/5 cm) over a flat portion of the anterolateral lower rib cage, the implanted stimulator, the indifferent electrode, and the connector to the phrenic nerve electrode are placed. The lead from the phrenic nerve electrode is tunneled subcutaneously and attached to this connector.

Avery Laboratories, Inc. (Commack, NY), which distributes the US-made device, favors implantation in the neck in adults, with a subclavicular receiver pocket fashioned via the same incision.

The Yale group, which has done much of the US clinical work, believes that tracheostomy in all patients is very important, even though the tracheostomy may be capped for much of the time. Those who have used positive pressure ventilation will already have the tracheostomy. It provides a reserve access to the airway in case of a problem with the pacing system. In addition, diaphragm pacing produces such a vigorous contraction of the diaphragm that it tends to close the glottis, and there is no coordinated opening of the glottis during stimulated inspiration. While this may be acceptable when the patient is awake, upper airway obstruction can result during sleep. Pacing patients with a tracheostomy are advised to remove the inner cannula of their (uncuffed) tracheal tubes during sleep.

Finnish Group

As with the Avery system, surgical implantation may be accomplished either in the neck or the thorax. However, placement in the thorax is preferred, as it offers more space and is sure to stimulate any accessory phrenic nerves, originating normally at C5 and C6 levels, which join the phrenic nerve below the level of the clavicle (16). The only additional step is to place and fix the anterior strip of the electrode over the nerve. Placement of the receiver-stimulators and the cables from the electrode array are similar to the Avery system. In carefully selected cases with normal function of nerves and muscles and the ability to increase the sigh volume by using the accessory ventilatory muscles in the neck, the tracheostomy may be closed, because suctioning is no longer needed. However, this group advises that the tracheostomy should not be closed if a pulse oximeter is not used during sleep (17). The frequency and severity of complications with a pulse oximeter or with a persisting tracheostomy are comparable.

Austrian Group

The Austrian group usually uses median sternotomy for implantation. The receiver is implanted in a subcutaneous pocket in the abdominal wall. The electrode leads are pulled through to the mediastinum, and four electrodes are applied to each phrenic nerve in the upper part of the mediastinum. Occasionally, electrode implantation has been performed on the phrenic nerve in the neck.

All quadriplegic patients treated with the Austrian phrenic pacemaker underwent a program to achieve auxiliary breathing via neck muscle contraction. As a result of such training, patients suffering from SCI below level C2 were able to breathe for at least 20 minutes spontaneously. These patients had their tracheostomies closed (18). No disadvantages have resulted from this maneuver; none of the tracheostomies have had to be reopened. Production of mucus diminished greatly. External compression of the thorax was sufficient for expectoration.

Commercial Devices

Three systems are commercially available for phrenic pacing: from Avery Laboratories in the United States, from Atrotech OY in Finland, and from MedImplant of Austria. Table I summarizes the characteristics of the systems.

Avery

The Avery I-107A device (Figure 1), used unipolar stimulation to each phrenic nerve with a remote indifferent electrode.
### Table 1.
Technical features of phrenic nerve stimulators.

<table>
<thead>
<tr>
<th>Device</th>
<th>AVERY I-107A (superceded)</th>
<th>AVERY I-110A</th>
<th>ATROTECH</th>
<th>MEDIMPLANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receiver size (mm)</td>
<td>46 (diam) x 16</td>
<td>30 (diam) x 8</td>
<td>49 (diam) x 8.5</td>
<td>56 x 53 x 14</td>
</tr>
<tr>
<td>Battery life (hr)</td>
<td>160</td>
<td>100</td>
<td>160-320 (12V)</td>
<td>24</td>
</tr>
<tr>
<td>8 (9V)</td>
<td></td>
<td></td>
<td>0.45 + 0.6 (12V)</td>
<td>0.8 + 0.62</td>
</tr>
<tr>
<td>Controller + battery weight (kg)</td>
<td>3.6</td>
<td>0.54</td>
<td>0.45 + 0.045 (9V)</td>
<td>0.45 + 0.045 (9V)</td>
</tr>
<tr>
<td>Controller size (mm)</td>
<td>179 x 114 x 97</td>
<td>146 x 140 x 25</td>
<td>185 x 88 x 28</td>
<td>170 x 130 x 51</td>
</tr>
<tr>
<td>Breaths/min</td>
<td>10-50</td>
<td>6-24</td>
<td>8-35</td>
<td>5-60</td>
</tr>
<tr>
<td>Pulse interval (ms)</td>
<td>35-170</td>
<td>40-130</td>
<td>10-100</td>
<td>25-170</td>
</tr>
<tr>
<td>Pulse width (microsec)</td>
<td>150</td>
<td>150</td>
<td>200</td>
<td>100-1000</td>
</tr>
<tr>
<td>Sigh possible</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Electrodes</td>
<td>Monopolar; bipolar</td>
<td>Monopolar; bipolar</td>
<td>Quadripolar</td>
<td>Quadripolar</td>
</tr>
<tr>
<td>No. of receivers to stimulate both hemidiaphragms</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

This device used trains of pulses, typically at a frequency of 7–10 Hz, lasting 1.3 sec and delivered 6 to 10 times per minute to produce contraction of the diaphragm and inspiration. The pulsewidth was 150 microseconds and currents were 1–3 mA. A higher inspiratory rate and shorter duration of inspiration is used for children, consistent with their physiology.

It has been found in recent years that body fluids can enter the Avery I-107A device, leading to stimulator failure between 1.5 and 3.0 years after surgical placement. In 1990, Avery Laboratories introduced a new model (I-110A) to overcome hermetic sealing problems with the original, which has not been available since the end of 1994. The new system is adapted from a pain control stimulator approved by the Food and Drug Administration (FDA) for diaphragm pacing. Uncoupling between receiver and antenna of the new system can occur with movements of only 1 cm, which could pose a potential clinical problem.

**Atrotech**

The nerve electrode of the Atrotech system consists of two connected strips of Teflon matrix, each strip containing two electrode contacts (Figure 2). One strip is placed in front of the nerve and the second behind the nerve, about 5 mm away longitudinally. Each of the four electrode contacts in turn serves as a cathode, and a contact on the opposite side of the nerve as an anode. Because of the separation of about 5 mm between anode and cathode, the stimulation is due to longitudinal rather than transverse current flow, reducing the charge requirements for nerve activation (19). When properly adjusted, sequential stimulation is intended to imitate natural activation of the nerve and reduce fatigue by recruiting groups of motor units asynchronously and allowing smooth contraction of the muscle at lower frequencies for each group of motor units.

At regular intervals the stimulation level is increased beyond that required for an adequate tidal volume. This causes a larger than normal tidal volume, known as a sigh. Thus, a larger muscle mass than that needed for normal tidal volume is conditioned and available if needed for increased metabolic demands (19).

The Atrotech control unit (Figure 2) provides for both everyday adjustments and special programming. It allows modification of the stimulated side of the diaphragm, alternating or bilateral stimulation, respiratory rate, and the sigh function.

During the conditioning phase, the clinician or engineer sets and modifies the stimulus parameters for each patient with a special programming unit. Later, this unit is rarely used (19). For each electrode combination, a threshold current and a current adequate to achieve a
normal tidal volume are set. The maximum current of each combination is then reduced to avoid overlap of excitation areas but still to produce an adequate tidal volume. The pulse interval is set between 40 and 60 ms, giving an overall stimulus frequency of 25–16 Hz. Smooth, graded diaphragm contraction is achieved by adjusting recruitment and frequency. Respiratory rate and inspiration duration are then adjusted over the conditioning period for individual patients. Stimulation is maintained during axial displacement of the transmitting coil by 4.5 cm and radial displacement by 2.5 cm.

**Figure 1.**
A. Diaphragm pacing apparatus includes transmitter, external antenna, implantable receiver, and the phrenic nerve electrode. The transmitter and the antenna coil, which is taped to the skin over the implanted receiver, remain outside the body.
B. The phrenic nerve electrode is placed at the level of the upper thorax and the implanted receiver is placed over a flat portion of the lower chest wall. Avery I-107A system, Avery Laboratories, Inc., Commack NY. (Reprinted with permission from TW Shields, ed., General Thoracic Surgery, Vol. 1, Fourth Edition, Williams & Wilkins, 1993.)

**MedImplant**

In 1973, the Austrian group started clinical stimulation of the phrenic nerve with single channel, nonimplantable devices. A technique called "carousel stimulation" for stimulation at different sites around the circumference of the nerve was patented by Thoma in 1976 (20) and was used for the first time in a human subject in 1979. Technical improvement led to the first implantable nerve stimulator for carousel stimulation in 1981, now provided by MedImplant (Figure 3).

This system uses sequential stimulation of four electrodes placed around each phrenic nerve; the electrode combination is changed with each inspiration, with the intention of reducing fatigue. The 0.2 mm epineural electrodes are stranded stainless steel wire (12 strands, 0.05 mm diameter), formed into 0.8 mm inner diameter loops and sutured to the epineurium with 8-0 prolene sutures using microsurgical techniques. The electrodes are applied as close to the nerve as possible without damaging neural structures (21–23).

Carousel stimulation allows stimulation at near physiologic respiratory rates: 11–17/min in adults and 15–25/min in children and infants. Duration of inspiration is set between 0.6 and 1.3 s to achieve a physiologic inspiration/expiration ratio. Mean minute
Volume is 150±24 ml/kg body weight which corresponds to mild hyperventilation with a PaCO₂ of approximately 30 mmHg (18). A stimulation frequency of 26 Hz is used to provide tetanic diaphragm contraction. Pulse trains are delivered with increasing current amplitude (threshold to maximum) to generate a smooth contraction.

The MedImplant device consists of one receiver (8 channels) and two multiple leads connecting to four electrodes on each phrenic nerve to activate both hemidiaphragms simultaneously (23). The external equipment consists of the control unit, the transmission coil, and various devices for power supply and battery charging. The control unit generates the stimulation information for both phrenic nerves. Up to 16 electrode combinations can be individually adjusted and activated for each nerve. The stimulation is maintained during transmission coil displacement of up to 6 cm in the axial direction and 3 cm in the radial direction.

The first version of the stimulation program is set up in the clinic. After training, the patient or an assistant can change the stimulation parameters of threshold current, maximum current, inspiration duration, and respiratory rate. Changes to pulse width and stimulation frequency must be made in the clinic.

Outcomes of Diaphragm Pacing

Avery Device

The I-107A stimulator has been in use for 25 years and has been implanted for respiratory pacing in almost 1,000 patients worldwide. At least five patients have been paced for more than 20 years (24).

At Yale, long-term follow-up of 14 quadriplegic patients who use bilateral low frequency stimulation recorded the longest use of the device as 15 years with a mean of 7.6 years (25). Tidal volume was maintained long-term without decrement, and the threshold and amplitude of stimulation required for maximum excursion of the diaphragm were unchanged over the long-term follow-up. Transition to full-time pacing required 3 to 9 months (25). Limited pathologic material has shown no evidence of significant damage to nerve, diaphragm, or lungs (26).

While the possibility exists that phrenic pacing improves life expectancy for people with high quadriplegia, there are no controlled studies. Carter reported 63 percent survival at 9 years with positive pressure ventilation (27,28). In the Yale experience, 100 percent of quadriplegic patients who completed the protocol (n=12) were alive at 9 years. Survival was probably due to avoidance of mechanical failure of ventilators, tracheal problems, and pulmonary infection—all benefits afforded by diaphragm pacing.

Persons with central hypoventilation, whose condition is not severe enough to require positive pressure ventilation, may develop chronic hypoxia with brain dysfunction and subsequent pulmonary hypertension. Comparative clinical trials are needed to determine the
influence of diaphragm pacing on this natural history, but they would have to be multicenter trials because of the small numbers of patients involved.

Atrotech Device

The Atrotech device had been used in 79 patients in 16 countries by the end of 1994 and is being implanted under Investigational Device Exemption from the FDA in the USA. This device has reduced the conditioning phase of the atrophied diaphragm from 6 to 2 months (29). Preliminary results also suggest that the sequential stimulation protocol of the Atrotech device allows longer fatigue resistant electrical ventilation. Clinical trials currently underway are expected to provide definitive data about fatigue resistance. Early commencement of full-time electrical ventilation for the patient with high quadriplegia means that he or she can be treated as a patient with low quadriplegia and thus receive the benefits of early rehabilitation (29).

MedImplant Device

Twenty-four patients have been treated with the MedImplant phrenic pacemaker between 1983 and 1994, mainly in Austria and Germany. Twenty-two suffered from total ventilatory insufficiency, and two were dependent on mechanical ventilation during sleep. Fifteen use electrophrenic respiration chronically during day and night; two, suffering from CAH, use electrophrenic respiration at night only; four patients could not be totally weaned off mechanical ventilation. Closure of the tracheostomy reduces the danger of pulmonary infection and allows the patient to speak and smell normally. Some patients regard this as the most remarkable improvement in their quality of life.

Intercostal Muscle Stimulation

Methods to activate the intercostal muscles of the rib cage have also been investigated, since those muscles contribute up to 40 percent of the vital capacity (30). The intercostal muscles contain both inspiratory and expiratory components: external intercostal muscles are inspiratory in function, while the internal intercostal are expiratory. However, in the upper rib interspaces, the external intercostal muscles are five to six times as thick as the internal intercostal muscles, and thus the upper rib cage musculature is predominantly inspiratory in function.

It is possible to activate the upper thoracic ventral roots supplying the intercostal muscles with a single electrode positioned on the epidural surface of the spinal cord (31). In animal studies, such an electrode at the T2 level achieved inspired volumes of 35–40 percent of vital capacity, comparable to volumes achieved by stimulation of the four upper thoracic spinal roots (32).

The technique of epidural spinal cord stimulation has been applied to ventilator-dependent quadriplegic patients with phrenic nerve injury (33). A quadripolar spinal cord electrode (8 mm x 45 mm: Medtronic, Minneapolis, MN) was placed on the ventral surface of the upper thoracic spinal cord following a laminectomy at T4-T5. In the month following electrode implantation, the four electrode terminals were tested to determine which two produced the greatest inspired volumes. In a second surgical procedure, the selected electrodes were connected to the cathodic leads of a radio frequency receiver implanted subcutaneously over the anterior rib cage. Anodic leads from the receiver were connected to indifferent electrodes, implanted subcutaneously over the back musculature.

A two-channel radio frequency transmitter (Medtronic Model #7520) delivered control signals through the skin. The transmitter allowed settings of cycle on-time, cycle off-time, pulse amplitude (0–10V), and stimulus frequency (8.6–32 Hz). Pulse duration was 0.15 msec. Pulse train rate (breaths/minute) could be varied between 6 and 23. At stimulation frequencies of 20–30 Hz, evidence of system fatigue was initially observed after 15–20 min. Over the course of a 20-week reconditioning program using gradually increasing periods of stimulation (Figure 4), it was possible to reduce stimulation frequencies gradually to 12–14 Hz, and tidal volume increased from about 200 ml to between 670 and 850 ml in three of four patients (33). The results for each patient in terms of the maximum tidal volume, vital capacity, negative inspiratory pressure, and time tolerated off mechanical ventilation are shown in Table 2.

While it was possible to generate large inspired volumes with intercostal pacing, the maximum duration off mechanical ventilation was relatively brief, ranging from 20 to 165 minutes, when using intercostal pacing alone (33). It is hypothesized that patients with partial diaphragm function, insufficient for phrenic nerve pacing alone, may benefit from combined intercostal and unilateral diaphragm pacing. In support of this hypothesis, previous work in animals suggests that combined intercostal muscle and diaphragm activation results in airway pressures (34) and inspired volumes
Figure 4.
Changes in maximum inspired volume during the reconditioning period for each patient. These changes generally were progressive increments in inspired volume production. The arrows in the figure of patient KM indicate when the dose of antispasmodic agents was reduced and then increased again.

Table 2.
Effects of intercostal pacing alone on maximum time off ventilatory support, inspired volume and negative inspiratory pressure.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Max. Pacing Duration Achieved (min)</th>
<th>Inspired Volume at 13 Hz (mL)</th>
<th>Inspired Volume at 32 Hz (mL)</th>
<th>Negative Inspiratory pressure at 32 Hz (cm water)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CM</td>
<td>20</td>
<td>500</td>
<td>850</td>
<td>-16.5</td>
</tr>
<tr>
<td>WW</td>
<td>60</td>
<td>450</td>
<td>710</td>
<td>-19.0</td>
</tr>
<tr>
<td>GL</td>
<td>165</td>
<td>550</td>
<td>670</td>
<td>-14.0</td>
</tr>
<tr>
<td>KM</td>
<td>15</td>
<td>300</td>
<td>470</td>
<td>-8.5</td>
</tr>
</tbody>
</table>

(35) equal to or greater than the arithmetic sum of those produced by either muscle group alone.

Combined intercostal and diaphragm pacing has been evaluated in two patients. A single-channel stimulator was used to activate the intercostal muscles and a commercially available phrenic pacer to activate one hemidiaphragm. A linking circuit was used to provide synchronous stimulation of both muscle groups. In the first patient in whom combined pacing was used, unilateral diaphragm stimulation resulted in a maximum inspired volume of 600 mL, while combined diaphragm and intercostal stimulation resulted in an inspired volume of 1,200 mL. This subject is now comfortably supported with combined pacing 24 h/day and is maintaining a PaCO\(_2\) of ~33 mmHg. The second patient is comfortably maintained off mechanical ventilation for about 12 h/day; she has chosen to remain on mechanical ventilation at night. Work is in progress to develop a single system to provide combined intercostal and diaphragm stimulation.

CONCLUSIONS

Ventilation by diaphragm pacing appears to provide both health and lifestyle advantages to the user (36,37). Freedom from the positive pressure ventilator reduces the risk of tracheal problems: tracheo-malacia, chronic infection, bleeding, and tracheo-esophageal fistula. These are caused by the cuffed tracheostomy tube and are often insurmountable. Mechanically ventilated patients can die suddenly if they become disconnected from the ventilator or if there is electrical or mechanical device failure. Such risks may be reduced for the person who uses electrophrenic stimulation. Added benefits of phrenic nerve pacing are the ability to speak more normally (provided the tracheostomy is closed, either surgically or with a stopper) and a preserved sense of smell. The phrenic pacser user can expect increased independence over the mechanical ventilator user; teenage patients have attended college, others have been gainfully employed, and many have traveled (27,38,39). Annual costs of supplies, total time in ventilatory care, and number of assistant hours are all less for phrenic pacing than for mechanical ventilation (40).

When Glenn reviewed the history of phrenic nerve stimulation for respiratory assist in 1988, 488 patients worldwide were known to have been treated with implantable devices (10). The current number is over 1,000. Phrenic pacing is a successful, life-sustaining technique proven over 25 years, but the electronic technology has lagged behind developments in other applications, such as heart pacing. It may be that the device manufacturers perceive the potential profit from phrenic pacing to be too limited to expend the effort to develop better systems.
Recommendations for Further Research

Further development of respiratory neuroprosthetic devices should address the need for:

- A fully implanted battery system of the type that exists for cardiac pacemakers. This would eliminate external antennas and the dangerous possibility of decoupling between transmitter and receiver.
- A system whose rate is responsive to metabolic needs. Current systems can be adjusted manually to alter the depth and rate of respiration; permanent monitoring of blood gas values would allow more sophisticated closed-loop control.
- A system that would coordinate stimulated breaths with the patient’s respiratory efforts, if any. Currently patients can be taught to synchronize opening of the glottis with stimulation of the diaphragm; it has been suggested that opening of the glottis might be sensed and used to trigger the phrenic stimulator.

Some of these principles have been implemented in cardiac pacemakers. Even though the population that can benefit from phrenic pacemakers is much smaller, there are opportunities for innovative engineers in both the commercial and academic arenas to work with physicians to develop totally implanted systems that would respond to metabolism and activity.

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