Long-Term Ventilatory Support by Diaphragm Pacing in Quadriplegia

WILLIAM W. L. GLENN, M.D., WADE G. HOLCOMB, B.E.E., RICHARD K. SHAW, M.D., JAMES F. HOGAN, B.S.E.E., KARL R. HOLSCHUH, M.D.

Thirty-seven quadriplegic patients with respiratory paralysis were treated by electrical stimulation of the phrenic nerves to pace the diaphragm. Full-time ventilatory support by diaphragm pacing was accomplished in 13 patients. At least half-time support was achieved in 10 others. There were two deaths unrelated to pacing in these two groups. Fourteen patients could not be paced satisfactorily, and 8 of these patients died, most of them from respiratory infections. The average time the 13 patients on total ventilatory support have had bilateral diaphragm pacemakers is 26 months. The longest is 60 months. Many of these patients are out of the hospital and several are in school or working. Injury to the phrenic nerves either by the initial trauma to the cervical cord or during operation for implantation of the nerve cuff was the most significant complication. Nerve damage from prolonged electrical stimulation has not been a problem thus far. A description of the pacemaker, the technique of its implantation, and the pacing schedule are reported.

It has now been nearly 5 years since total support of ventilation was first accomplished in a quadriplegic patient by means of bilateral, programmed electrical stimulation of the phrenic nerves (diaphragm pacing) (3). That patient continues to do well, unaided by mechanical respiratory support. He has been living at home since May, 1971, and is gainfully employed. Diaphragm pacing has subsequently been applied with varying success to 36 other patients with respiratory paralysis accompanying quadriplegia. Nine of these patients were treated in our institution, the remainder in a number of other institutions. As far as we know, this is the total experience with diaphragm pacing in quadriplegic patients.

The Clinical Series

The collected series of 37 patients with quadriplegia who could be paced was reviewed. There were 24 males and 13 females whose ages ranged from 4 to 71 years. The largest proportion of cases were young adults, in the age group of 15 to 30 (Fig. 1). Quadriplegia was caused by violent injury to the spinal cord in all but 3 patients, of whom two developed complete paralysis from ischemia of the cord following surgical procedures attempting to relieve osseous compression of the cord and one developed incomplete paralysis as a consequence of syringomyelia. The last was the only instance of incomplete quadriplegia in the series (Table 1). In 27 patients the lesion involved predominantly the C1-C2 segments of the cord, in the other 10 patients the C3-C5 segments.

The cuff electrode and the receiver were implanted two months to 11 years after the initial injury. In the patients who had normal nerves positive pressure ventilation could be omitted for at least part of the time within one month after pacing was started. Delay of full-time support by pacing was sometimes the result of emotional instability, especially prevalent in the children.

Full-time pacing was accomplished in 13 patients. These patients used no other form of ventilatory support and had no ventilation except what they could achieve with their neck muscles. In 10 other patients ventilation was provided by pacing at least 50% of the time. Two of these were paced for 18 hours daily and did not require


Supported by U.S. Public Health Service grants HL04651, HL14179, and RR00125, by the Culpeper Foundation, and by Mrs. Jane Fetter.
positive pressure breathing; one, the patient with syringomyelia, was able to support her respirations voluntarily for 6 hours daily, and the other patient, who had a transection at C2, used a pneumobelt while sitting for 6 hours daily. Total ventilatory support was thus provided by diaphragm pacing for 50 to 100% of the time in 23 patients, 62% of the series. Two of these patients (9%) have died; one, who was on full-time pacing, died as a result of meningitis secondary to a sacral decubitus and the other died in his sleep, presumably as a result of respiratory arrest, 4 months after resumption of voluntary respiration and discontinuation of pacing.

In the remaining 14 patients in the series ventilatory support for as much as 50% of the day could not be achieved. Eight of these have died. Most of the deaths resulted from respiratory tract complications (Tables 2 and 7).

The average time elapsed since implantation of the pacemaker in the 13 patients whose ventilation was supported totally by diaphragm pacing is 26 months; the longest period of continuous support is nearly 5 years (Fig. 2). The time of the beginning of full support by diaphragm pacing after implantation of both phrenic nerve stimulators was usually 2 to 4 months but could not definitely be ascertained in all cases.

Failure to pace or ineffective pacing resulting from malfunction of a pacemaker component was usually due to shorting out of electronic components in the receiver because of flooding, or to a breakage of the antenna connector. No case of failure due to breakage of an electrode was reported in the series (Table 3).

Injury to one or to both phrenic nerves was the major cause of failure of the attempt to support ventilation. Four nerves showed no response, i.e., diaphragm contraction, to direct stimulation at operation and it must be presumed they were destroyed by the initial trauma. In 11 instances absence or weakness of the response to neural stimulation was attributed to iatrogenic trauma during application of the cuff electrode to the nerve. In a number of other cases there was less than the expected response and in these the nerve may either have been damaged by the initial injury or by operative manipulation. Partial or complete recovery of a nerve injured at operation was seen in two cases 12 and 16 months postoperatively.

Infection of the implanted unit occurred in 5 cases. In one case the infection involved only the site of the electrode junction. The junction point was exposed, thoroughly cleansed with povidone iodine and reim-

---

**TABLE 1. Causes of Quadriplegia**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automobile or motorcycle accident</td>
<td>16</td>
</tr>
<tr>
<td>Sports injury</td>
<td>14</td>
</tr>
<tr>
<td>Gun shot wound</td>
<td>4</td>
</tr>
<tr>
<td>Disease (syringomyelia)</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative ischemia of cord</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

**TABLE 2. Results**

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full time pacing</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Part time pacing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50%</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>37</strong></td>
<td><strong>10</strong></td>
</tr>
</tbody>
</table>
planted in an uncontaminated subcutaneous pocket. Prior to its closure the wound was thoroughly irrigated with antibiotics, then systemic antibiotic coverage given for several weeks. In cases where the infection involved the electrode cuff site, removal of the cuff was necessary in order to control the infection.

The effects of long-term electrical stimulation on neural function could be evaluated only in the 9 patients treated in our clinic and not in all those in the collected series. Pacing provided total ventilatory support for 4, and support for at least 50% of the time for 3. The other two could not be paced adequately; one of these died, as did one who was fully supported by pacing but developed meningitis as previously noted. The adequacy of pacing was assessed periodically by analysis of arterial blood gases, studies of tidal volume, measurements of diaphragmatic excursions and determination of the current required to achieve minimal (threshold) and maximal contraction of the diaphragm.

The 7 patients who were paced 50 to 100% of the time showed nearly normal arterial blood gases when these were measured at the beginning and end of any 12-hour pacing period. Hyperventilation was common as evidenced by the somewhat lower than normal levels of CO₂ (Table 4).

The minute volumes in the patients totally supported by pacing were usually in the normal range, 5 to 10 liters per minute (Tables 4 and 5). At the start of treatment they were sometimes lower than normal but increased with daily pacing.

The threshold level noted initially at operation was invariably lower than levels measured subsequently. There was a rise for about 6 months from the start of pacing and then a slow fall over the next few years. In the longest-paced quadriplegic, thresholds at operation and after 5 years of pacing were 1.5 mA and 3.04 mA respectively on the right side, and 0.7 mA and 1.02 mA respectively on the left side (Fig. 3).

Diaphragmatic excursions during pacing were observed fluoroscopically and a ciné record made. When the nerve being stimulated was undamaged and the patient was lying supine, a descent of the diaphragm of 6 to 10 cm was the usual finding. Restriction or absence of movement was evidence of a damaged nerve.

Postmortem examination of the phrenic nerves of two quadriplegic patients was made by Drs. J. Kim and E. Manuelides.* Microscopic examination of the nerves from one of these patients showed focal demyelination and macrophages at the site of the electrode cuff. The patient, a 36-year-old man with a C2-C3 transection, had been paced for less than three months when he died suddenly. His ventilatory exchange on pacing had been

---

* This material together with the results of microscopic examination of the stimulated nerves of four other patients with Ondine's Curse is being prepared for a detailed report by Dr. Kim and associates.
poor from the day of operation and full-time pacing was never achieved. The second patient, a 29-year-old man with a C2 transection, achieved full-time support with no difficulty and pacing of each side gave a minute volume of 10 to 14 liters. He died of meningitis 20 months from the start of pacing. Careful examination of both nerves failed to reveal any significant abnormality.

Materials

The Diaphragm Pacemaker

The radiofrequency (RF) unit used for pacing all patients in this collected series was developed at Yale in the early 1960's and as modified since then has been described. Briefly, it consists of an external battery-powered transmitter, an antenna placed on the skin, a radio receiver embedded subcutaneously beneath the antenna, and platinum electrodes which surround and conduct current to the phrenic nerve. The transmitter creates a series of 33 radiofrequency pulses of short duration spaced by intervals of 37 msec. This series of pulses may be adjusted (in the transmitter) so that the first pulse in the series matches the threshold to stimulation and the 33rd pulse provides optimal diaphragmatic motion. Current delivered by the receiver to the nerve increases about 7 μamp per μsec of pulse duration. Exact conversion characteristics of the receiver can be calibrated prior to implantation. This design provides capability of generating current from 0 to 10 mA from a receiver with a constant current characteristic. Threshold currents are determined from the receiver calibration.

Application of this pacemaker to the 9 patients under our care and review of the total series have revealed to us certain points relative to the conduct of diaphragm pacing that bear emphasizing.

Battery Life. A fresh 9-volt alkaline battery will operate the pacemaker for about 40 hours. At the end of each 12-hour period of use the battery should be checked for the remaining charge by an instrument provided for this purpose; eight volts or more are necessary for safe pacing. Larger, rechargeable batteries (lead acid, such as a 12-volt motorcycle battery), carried separately in the patient's wheelchair or kept by the bedside, may be more convenient for certain patients.

Transmitter. The variable potentiometer regulating the current is fragile and must be turned carefully. Other adjustments on the transmitter (stimulus slope, pulse width, and respiratory rate) are manipulated only according to the manufacturer's instructions. No attempt should be made to increase the minute volume by increasing the rate beyond 17 per minute or the current beyond that which at fluoroscopy produces a maximal contraction.

Antenna. The connector between the antenna and the transmitter is especially vulnerable to rough handling; care must be exercised to line up the ends correctly when making connections. The antenna is held to the skin overlying the receiver with one or two strips of paper tape; this skin should be cleansed daily.

Receiver. The most common complication we have encountered with the unit during diaphragm pacing has been failure of the radio receiver. This has usually occurred during the first two years after implantation. Impending failure is most frequently heralded during pacing by a sharp pain over the electrode site in the neck or by erratic pacing. Occasionally pacing stops abruptly without warning. It is therefore essential that patients dependent upon pacing be provided with an alarm to summon help. Should confirmatory tests of electronic equipment indicate failure of the receiver, the latter must be

<table>
<thead>
<tr>
<th>Operative</th>
<th>Probable nerve injury</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Pacemaker</td>
<td></td>
</tr>
<tr>
<td>Receiver</td>
<td>Antenna connector breakage</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 3. Complications

<table>
<thead>
<tr>
<th>Side paced</th>
<th>V/E (liters/min)</th>
<th>Pco2 (mm Hg)</th>
<th>Po2 (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At start</td>
<td>5.8</td>
<td>24</td>
<td>108</td>
</tr>
<tr>
<td>After 12°</td>
<td>5.9</td>
<td>25</td>
<td>98</td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At start</td>
<td>6.2</td>
<td>27</td>
<td>103</td>
</tr>
<tr>
<td>After 12°</td>
<td>5.5</td>
<td>27</td>
<td>101</td>
</tr>
</tbody>
</table>

Table 4. Ventilatory Studies

Data on Patient K. deS., a 19-year-old quadriplegic woman, are given. The dates of phrenic nerve implantation are as follows: left side, Jan. 18, 1971; right side, Jan. 10, 1972. This study was performed in April, 1973. (After Glenn et al.: J Thorac Cardiovasc Surg 66:505, 1973).

Addendum: For more than 3 years, this patient has followed a schedule in which pacing of the sides was alternated at each breath for 14 to 16 hours daily and was of both sides simultaneously, to enable sitting, for 8 to 10 hours daily. On this schedule, ventilatory studies were repeated in December 1975: V/E, 4.61 liters/min (average of 5 measurements); Pco2, 28.8 mm Hg; Po2, 114 mm Hg; the current required to produce minimal contractions (threshold) had decreased in the interval to less than 1.5 mA on both sides.

Table 5. Ventilation During Diaphragm Pacing

<table>
<thead>
<tr>
<th>Date</th>
<th>Body position</th>
<th>Voluntary assistance</th>
<th>Minute volume 1/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971</td>
<td>Reclining</td>
<td>no</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>yes</td>
<td>11.4</td>
</tr>
<tr>
<td>1975</td>
<td>Reclining</td>
<td>no</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>yes</td>
<td>11.5</td>
</tr>
</tbody>
</table>

Data given for J. C., age 38, following C1-C2 injury.
replaced immediately; stimulation of the opposite nerve will support the patient only 12 to 18 hours before nerve fatigue begins to impede ventilation. Provisions must always be made to return to endotracheal positive pressure ventilation in the event of pacemaker failure.

Electrodes. Malfunction of the cuff electrodes has not been a problem except from infection or from trauma during implantation, as described above.

Methods

Schedule for Operation

When damage to the spinal cord and resulting respiratory paralysis appear to be permanent, implantation of a pacemaker should be considered. Implantation is delayed at least two to three months after injury, however, to allow for a possible return of diaphragmatic function, as was seen in a few patients in the series several months or more following the cord injury, and allow time for the patient to become thoroughly acquainted with the use of positive pressure ventilation in the event of pacemaker failure. Respiration is provided in the meantime by positive pressure ventilation.

Viability of the Nerve

The primary requirement for successful pacing is viability of the phrenic nerves. This may be ascertained preoperatively by percutaneous stimulation of the nerves where they pass over the scalene muscles. The technique used by Sarnoff is employed (Fig. 4). With practice the nerves can readily be located. A quick hiccup-like contraction of the diaphragm on the side of stimulation is evidence of the integrity of the nerve and if the contraction is vigorous most of the neurons are probably viable. Failure to obtain diaphragmatic contractions upon stimulation usually indicates non-viability but when in doubt one should explore the nerve directly. The surgeon exploring the nerve must be prepared to place an electrode upon it if he finds it viable. Assessment of neural function by studies of conduction time using percutaneous stimulation according to the technique of Davis is advised in the preoperative period to provide a comparison after placement of the nerve in the cuff.

Operative Techniques

Attachment of Cuff and Receiver

The technique for applying the cuff electrode and installing the radio receiver in the 9 Yale patients is that which we have used in our clinic since 1968. Briefly, it is as follows:

In the adult, under local anesthesia, a 4-inch transverse incision is made one inch above and parallel to the clavicle. The phrenic nerve is isolated where it crosses the scalenus anticus muscle and an electrode cuff is placed around it. Insulated wires connect the cuff to the radio-frequency receiver implanted in the subcutaneous tissue of the anterior chest wall. In the child under 12 years of

![Fig. 3. Threshold to stimulation (minimum current required to produce diaphragmatic contractions) in a 38-year-old C1-C2 quadriplegic over a 5-year period. The current required to stimulate the right diaphragm soon after pacing was started was uniquely high but movement of the two sides of the diaphragm was the same.](image-url)
age whose neck may be too short to accommodate the cuff, it can be placed at thoracotomy and at a site as far from the heart as is feasible in order to lessen the chance of stimulation-induced fibrillation.

Precautions with Cuff Application. Damage to the phrenic nerves during implantation of the electrode is the most serious complication and was apparently the cause of failure to pace in 11 nerves (16% of the nerves stimulated in the collected series). For this reason certain points in the technique of application\(^4\) deserve reemphasis. 1) Sterilization of the cuff electrode must be by autoclave only; a residue on the cuff of ethylene oxide or chemicals ordinarily used for sterilization could severely injure the nerve. The receiver, which does not come in contact with the nerve, may be sterilized by ethylene oxide or in the autoclave; we prefer gas sterilization as it subjects the electronic components to less heat than does autoclaving. 2) The electrode-receiver assemblies, two of which are required in the quadriplegic for stimulating both phrenic nerves, are each implanted at a separate operation to provide time for meticulous dissection and to lessen the danger of infection. 3) Identification of the phrenic nerve where it passes over the scalene muscle is accomplished atraumatically with single stimulation of 1 to 10 volts. Of course, local anesthetic must not be instilled in the vicinity of the nerve. 4) Isolation of the nerve and placement of it within the cuff is carried out with utmost care and gentleness. The pre scalene fascia is not removed from the nerve. Instead, parallel incisions about 15 mm long are made through the fascia two to three mm on both sides of the nerve, with care taken to preserve the perineural blood supply. With the nerve elevated slightly by a rightangled clamp or nerve hook, the posterior lip of the cuff (5 mm ID) is slipped behind the nerve; traction on a suture attached to the posterior lip and inserted behind the nerve will aid this. It is at this point that injury is most apt to be inflicted. The most common injury is impaling the nerve or perineural tissue on the tip of the platinum electrode as it is passed behind the nerve. Once the nerve is in place in the cuff it should lie loosely and have no angulation where it enters and leaves the cuff. 5) Cephalad orientation of the horn of the cuff, marked with a red thread, is important to insure stimulation of the nerve by the cathode electrode.

When a diaphragm responds at operation but fails to be paced at any time postoperatively iatrogenic injury is suspected. It is probably wise to remove the cuff in such cases and let the nerve recover, which may take 6 to 18 months. The cuff could then be reimplanted at thoracotomy at a point lower on the nerve. Removal of the cuff is not obligatory for recovery if the cause of the injury has been removed.

Implantation of Receiver. Following application of the cuff electrode to the phrenic nerve a second transverse incision, 3 to 4 inches long, is made at the costal margin in the mid or anterior axillary line to create a subcutaneous pocket which is then developed cephalad 3 to 4 inches deep. A third incision, two inches long, is made at the level of the fourth rib in the mid clavicular line to provide access to the silastic-covered wires from the cuff electrode above and the receiver below. The wires from the receiver and from the cuff are brought towards each other within subcutaneous tunnels. Subcutaneous passage of the wires from the cuff electrode is facilitated by passing a plastic chest tube (#28F) through the third incision, then into the neck wound above and threading for a short distance the tip of the electrodes into the open end of the tube. When the tube is withdrawn through the incision the electrode wires, except for the terminal segments, remain in the tunnel and the ends become accessible externally for connecting to the ends of the receiver electrodes, passed subcutaneously from below in like manner. Following insertion of the radio receiver into its pocket, connections are made between the electrode wires of the receiver and cuff, with anodes and cathodes matched according to identifying red markers. The electrode wire connection is further secured with a monofilament synthetic ligature. The junction and any excess wire are implanted in a Teflon (0.5 mil thick) bag subcutaneously for easy accessibility should replacement become necessary. All incisions are closed and dead space obliterated with multiple interrupted sutures of plain
FIG. 5. Teflon tracheostomy button used to plug the tracheostomy stoma during diaphragm pacing (Quinton Instrument Co.).

catgut, with care not to incorporate the electrode wires in the sutures. The integrity of the system is checked by stimulation with a sterile antenna prior to closure of the wounds. Nerve-electrode contact is assured by flooding the neck wound with saline.

Pacing Schedule

To allow time for postoperative edema to subside, stimulation of the nerve is not begun for at least 12 days after implantation of the unit. If the stimulators have been implanted separately, as we advise, one side will be about two weeks behind the other on the pacing schedule. When pacing is begun the patient is fluoroscoped and the extent of diaphragm motion measured for future comparison.

The diaphragm in many quadriplegics is weakened from prolonged inactivity and must be conditioned through a gradual lengthening of the periods of stimulation. Generally, at the beginning, stimulation is done for 5 minutes of each hour. Tidal volumes are measured at the start and finish of each period of stimulation. If the tidal volume at the end of the period is 75% or more than at the beginning, the length of pacing can be increased. Usually we have increased it one to two minutes per hour per day until the diaphragm is being paced 30 minutes in each hour. The periods of pacing can then be lengthened by 5-minute per hour increments daily. Positive pressure ventilation is continued during this conditioning of the diaphragm or, if the minute volume is adequate (>5 l/min in adults), it can be discontinued during the periods of pacing. Usually diaphragm conditioning is done only during the waking hours, the respirator being used during sleeping. When one hour of pacing is reached with an adequately maintained minute volume a similar period of rest is scheduled. Pacing then is increased by 15-minute increments daily until 6 hours is reached. This is followed by a similar rest period. At this point it is usually possible to increase pacing up to 8-, 10- and 12-hour periods. When pacing on each side has been extended to 12 hours, while producing satisfactory minute volumes and normal arterial blood gases, the patient can be taken off the respirator completely. This weaning has usually taken from 2 to 3 months.

Sitting during pacing causes the minute volume to drop sharply. It can sometimes be raised by wearing an abdominal belt to elevate the diaphragm, which increases the effectiveness of pacing, and/or by pacing both sides simultaneously. An alternative is the use of a pneumobelt without pacing, a practice carried out by several patients in the series.

Once the maximal stimulation time has been established, several schedules for maintaining it have been adopted. To those patients who respond normally to stimulation of either side of the diaphragm, we recommend pacing each side alternately, 12 hours at a time. A few patients prefer to alternate pacing with each breath. Both sides of the diaphragm may be paced simultaneously for as long as 8 hours daily. When only one side can be paced, stimulation of the phrenic nerve for longer than 16 hours daily is not recommended.

Until full-time pacing is established a tracheostomy tube must remain in place. Even when positive pressure ventilation is no longer required, the tracheostomy stoma must be kept open for occasional suctioning, since these patients cannot cough effectively, and also for a reinstitution of positive pressure breathing should the pacemaker fail or ventilation become inadequate as with severe bronchitis or pneumonia. Following removal of the tube a Teflon button is carefully fitted to the tracheostomy stoma* (Fig. 5).

Discussion

This review of 37 quadriplegics who have undergone diaphragm pacing has pointed up certain problems in the

<table>
<thead>
<tr>
<th>Conduction time</th>
<th>Right side msec</th>
<th>Left side msec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Postop</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 mon</td>
<td>9.6</td>
<td>11</td>
</tr>
<tr>
<td>16 mon</td>
<td>10</td>
<td>10.6</td>
</tr>
</tbody>
</table>

Data given for R. S., age 52 years, 11 months following C3-C4 injury.

* Obtainable from the Quinton Instrument Co., 3051 44th Ave., W., Seattle, Washington. The diameter of the tracheal stoma and the distance from the skin to the trachea should be measured and furnished the supplier.
Fig. 6a. Current required to produce minimum contractions (threshold) of the diaphragm in the authors' series of patients with central alveolar hypoventilation (Ondine's Curse) and with quadriplegia. In one quadriplegic patient the threshold on the right rose to 5mA two months postoperatively and then decreased markedly. Threshold values for this one nerve are not included on this graph, but are shown in Fig. 3.

selection of patients, in the techniques of applying the apparatus, especially to the phrenic nerve, and in the management of patients once diaphragm pacing has started.

In the selection of patients it was apparent, and expected, that the level of injury to the cervical cord would influence the viability of the phrenic nerves, reflecting the fact that the phrenic nerves arise from the anterior horn cells in the C3, C4 and C5 segments. Damage to these segments impaired or totally destroyed function of the phrenic nerve in some of the patients and electrical stimulation of the peripheral nerve in such was,
of course, ineffective. When C3, C4 or C5 segments are damaged and full-time ventilatory support is needed but cannot be achieved by pacing the diaphragm, pacing for even 50% of the time will reduce the risk of respiratory complications and increase the patient's mobility.

The resumption of voluntary respirations following respiratory paralysis secondary to cord injury was seen twice in the series. One patient has continued to do well though paralysis below the C5 level persists. The other patient died in his sleep, presumably from respiratory arrest, 4 months after resumption of voluntary respiration. It is likely that weakness of respiratory muscles persisted and although ventilation was adequate during waking hours apparently it was not while he slept. As the ventilatory response to hypercapnia or hypoxemia may be depressed in patients with chronic ventilatory insufficiency, night-time pacing must be continued until repeated blood or alveolar gas measurements show that ventilation during sleep is adequate.

Operative trauma to the phrenic nerve was a serious problem. This is not surprising when one considers with what ease this nerve can be damaged. Undoubtedly the problem is due in large part to the difficulty of applying the cuff to the nerve and fixing it to the tissue. Nevertheless, the fact that total ventilatory support which is dependent upon an essentially normal response of both phrenic nerves to stimulation has been accomplished in 13 patients for an average of 26 months is indicative that the cuff electrode can be placed atraumatically. Modification of the design of the electrode to make it easier to apply to the nerve is being actively pursued in the research laboratory.

If a nerve is damaged at operation the injury may not be recognized until pacing is attempted 12 to 14 days later. If nerve function is impaired it is probably advisable to explore the cuff and remove it if it appears to be compressing the nerve. When injury to the nerve is not evident the cuff may be left in place. Two quadriplegic patients whose nerves were probably injured at operation and in whom the cuff was not removed showed partial to complete return of function 12 to 16 months later. Conduction time in the phrenic nerves should be determined before operation and periodically thereafter. In one quadriplegic patient with a suspected injury of the left phrenic nerve at operation the conduction time remained prolonged postoperatively whereas the conduction time in the normal right nerve showed the usual postoperative shortening.19 Sixteen months later there was evidence of return of function in the injured nerve by an increase in diaphragmatic motion and the phrenic nerve conduction time was now about the same as in the opposite nerve (Table 6).

Injury to the nerve due to the electrical stimulus has not been demonstrated in these patients. The average current required to cause minimal contraction of the diaphragm (threshold) increased for the first 6 months of pacing and has since declined. The relatively small number of observations made on our 9 quadriplegic patients was compared with a larger number made on 31 patients with central alveolar hypoventilation paced nightly for 10 to 14 hours. Except for the uniquely high level of current required to pace one side of the diaphragm in one of the quadriplegics (Fig. 3), the current requirements of the quadriplegics and the patients

![Graph](image-url)
with Ondine’s Curse have been almost identical (Fig. 6). On the other hand, the current required for maximal contraction of the diaphragm was definitely greater in the quadriplegic patients (Fig. 7).

The length of time from the injury to the start of pacing did not appear to influence the length of time required to achieve full-time (12 hour) pacing. In fact, the patient in whom this interval was longest, 11 years, required only 6 weeks of conditioning to achieve complete support of respiration for 12 hours on stimulation of the right nerve. Satisfactory pacing on stimulation of the left nerve was not achieved, either because of injury to the nerve or its cell bodies in the initial accident or traumatization of the nerve at operation. Several other patients whose injury was received 3 or 4 years prior to phrenic nerve stimulation achieved full-time ventilatory support by pacing within a few months.

It is significant that 8 of the 10 deaths in this series occurred in patients in whom it had not been possible to establish satisfactory pacing. It is also significant that 5 of the 8 deaths were due to respiratory tract infections (Table 7). The incidence of respiratory infections in the quadriplegic who is on full-time support by diaphragm pacing and who has a plugged tracheostomy stoma is probably no greater than in the normal population.

Pain on diaphragm pacing is an abnormal finding. It may appear in the neck if the pacing current is high. The sudden onset of pain in the neck during stimulation, as was observed in two patients, was associated with a malfunctioning receiver and was corrected by replacement. Pain in the chest or abdomen was reported by two patients. In both cases operative injury to the phrenic nerve had been suspected.

The principal aim of most of these individuals is to leave the hospital. As one expressed it for all when asked how her pacemaker helped her, she said, “It keeps me out of the hospital and off the MA-1.” Nevertheless, the rehabilitation of the quadriplegic who is no longer completely dependent on a positive pressure respirator creates new problems for the patient and his family. The emotional adjustment can be difficult, especially for the younger patients, but where there is an understanding and compassionate family these patients can be encouraged to participate in many activities, including school and even gainful employment. It now becomes the responsibility of the family to take those precautions necessary to protect the patient from infections, particularly those arising in the urinary tract and secondary to decubitus ulceration. The patient and his family should be thoroughly familiar not only with the operation of the positive pressure apparatus, which must always be in readiness in case the pacemaker fails, but also with the operation of the pacemaker. These patients must be provided with a fail-safe alarm system.

### Table 7. Causes of Death

<table>
<thead>
<tr>
<th>Infection</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>5</td>
</tr>
<tr>
<td>Septicemia</td>
<td>1</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>3</td>
</tr>
</tbody>
</table>
Conclusions
A new attitude toward the quadriplegic with respiratory paralysis appears to be justified. It is not known for how long the phrenic nerves can withstand electrical stimulation by the present method. Five years is a good beginning. It can be expected that more sophisticated, less traumatic techniques of stimulation of the peripheral nerves will be developed that will provide electrical substitution indefinitely for central nervous system control of respiration.

Acknowledgments

References

Discussion

DR. A. ROBERT CORDELL (Winston-Salem): Being able to place an electrically stimulating electrode around the phrenic nerve without producing ischemia or loss of its function is an accomplishment.

I'd like to pose a couple of questions to Dr. Glenn, and the first is: Can indications for the use of diaphragmatic pacing be extended to include some of the patients who might be comatose on a supposedly temporary basis after trauma, for example, or in patients who have chronic obstructive pulmonary disease, or in certain other trauma victims, even including some patients with chest trauma who might be allowed to be taken off continuous ventilatory control by virtue of this adjunct?

My second question is: Could the concept of so-called "demand use" of diaphragmatic pacing work to advantage in some patients with, for example, the possibility of sensing respiratory rate or blood gases as a method of long-term, continuing control, when necessary by this method?

DR. GILBERT S. CAMPBELL (Little Rock): I first became interested in prolonged ventilatory support when I was in Minnesota during a polio epidemic in 1947. It's impossible to recognize the real worth of this paper unless you realize that patients with chronic hypoventilation are literally imprisoned, either in tank-type respirators in the old days, or attached to volume controlled ventilators in today's time.

DR. LESLIE R. BRYANT (New Orleans): I rise primarily to ask Dr. Glenn a couple of questions about the indications for use of the diaphragm pacers. I think many of us are unsure about the selection of patients who might benefit. The publication of this paper may encourage some of our colleagues to request that we see patients who are potential candidates, and I want to ask Dr. Glenn to give us his thoughts in two categories.

To illustrate the questions, my service was asked recently to see a 40-year-old woman at Charity Hospital in New Orleans, who has been the victim of demyelinating disease, and who is dependent on the respirator for her life. The two questions are: Is there any relationship between the patient's socioeconomic background and the likely success of diaphragmatic pacing? And, are the demyelinating nervous diseases contra-indications for the application of phrenic respiration?

You mentioned one case, I believe, of syringomyelia, but I believe it would be helpful for me and for others to know whether you have formed some idea in your own mind about the indications for phrenic respiration in demyelinating diseases.

DR. W. W. L. GLENN (Closing discussion): Dr. Cordell, so far as temporary pacing is concerned, I do not think that there is any place for the techniques that we have illustrated here today for a temporary problem, because of the possibility of injury to the nerve. It may be that temporary pacing will have a place if it can be perfected by the transvenous route, such as has been advocated by Escher, Daggett and others. But I think that at present we can only say that positive pressure respiration is probably a safer technique for the treatment of acute, reversible hypoventilation.

With regard to the development of a demand diaphragm pacemaker, this is entirely feasible. As a matter of fact, only a few days ago we studied a patient with Ondine's Curse whose pCO2 built up very rapidly when he went to sleep. By continuously sampling the air from his nose and passing it through a CO2 analyzer it was a simple matter to construct a circuit to turn on the diaphragm pacemaker when the CO2 rose above a certain level.