Management of Airway Clearance in Neuromuscular Disease

Louis J Boitano MSc RRT

The clearance of airway secretions from the lungs is normally supported by the mucociliary escalator and by cough. These protective mechanisms provide an effective means of pulmonary-hygiene maintenance in healthy individuals. Patients with neuromuscular disease that affects the respiratory pump (the muscles of breathing) can experience mild to profound limitation in both ventilation and cough. Neuromuscular respiratory insufficiency, when left untreated, can substantially impact quality of life and life expectancy. In most cases of neuromuscular disease, respiratory failure and pneumonia are the primary causes of death. Invasive mechanical ventilation and tracheal suctioning have been successfully used when needed to support respiratory insufficiency in this population. These modalities, though supportive, have been associated with substantial morbidity when used in patients with neuromuscular disease. The advent of noninvasive ventilation as a means of supporting chronic neuromuscular respiratory insufficiency has spurred the development of noninvasive cough-augmentation therapy to support airway clearance. Unfortunately, the need to support cough clearance is not always addressed, and few guidelines for the management of cough insufficiency have existed until relatively recently. An understanding of neuromuscular respiratory pathophysiology and the modes of effective noninvasive cough support are key in the evaluation and management of neuromuscular diseases. This review is meant to provide a basic understanding of cough mechanics, and the pathophysiology and management of neuromuscular cough insufficiency. *Key words: cough, neuromuscular, mechanical in-exsufflation, noninvasive, pathophysiology, airway clearance.* [Respir Care 2006;51(8):913–922. © 2006 Daedalus Enterprises]

Louis J Boitano MSc RRT is affiliated with Respiratory Care Services, University of Washington Medical Center, Seattle, Washington.

Correspondence: Louis J Boitano MSc RRT, Department of Respiratory Care Services, University of Washington Medical Center, Box 356166, 1959 NE Pacific Street, Seattle WA 98195. E-mail: boitano@u.washington.edu.

Introduction

Neuromuscular-induced respiratory insufficiency has long been associated with morbidity and mortality in patients with neuromuscular disease. Chronic and progressive neuromuscular disease can result in various degrees of ventilatory impairment, atelectasis, and cough insufficiency. All of these respiratory sequelae can predispose patients with neuromuscular disease to complications associated with respiratory infection. Cough insufficiency may contribute the greatest limitation to the respiratory health of neuromuscular patients with chronic respiratory insufficiency. Diagnostic testing has been developed to evaluate cough strength and implement timely cough-augmentation therapy in the preventive respiratory management of patients with neuromuscular respiratory insufficiency.

The goals of this paper are: (1) to review cough mechanics and the pathophysiology of neuromuscular-induced cough insufficiency, (2) to describe the diagnostic testing that has been used to evaluate cough strength, (3) to describe and compare the different modalities currently used for cough augmentation, (4) to discuss the limitations to cough-augmentation therapy, and (5) to discuss the use of secretion-mobilization and cough-augmentation therapies in the airway-clearance management of neuromuscular patients with respiratory insufficiency.

Cough Physiology and Mechanics

The function of cough is to clear inhaled foreign materials captured in the mucociliary system, retained secretions or excessive secretions associated with respiratory infection or impaired mucociliary clearance, and aspirated materials. Cough is a complex maneuver that is initiated either voluntarily or by the stimulation of cough receptors located primarily in the central airways. Mechanical irritant cough receptors are sensitive to touch and displacement, and may also be sensitive to temperature. Mechanical receptors occur in the greatest density in the posterior trachea, larynx, and carina, and decrease in density in the central distal airways. Chemical irritant cough receptors are sensitive primarily to noxious gases and fumes and occur in greater density in the distal central airways and in greater density at the airway junctions. The vagus nerve is thought to be the primary afferent pathway to the cough center that initiates the cough response. The efferent nerve impulses of the cough reflex are transmitted through the phrenic nerve and other spinal motor nerves, and to the larynx through vagal nerves that stimulate the cough response.[1]

The sequence of phases in a cough maneuver can be classified as inspiratory, compressive, and expiratory (Fig. 1). In the initial inspiratory phase, active abduction of
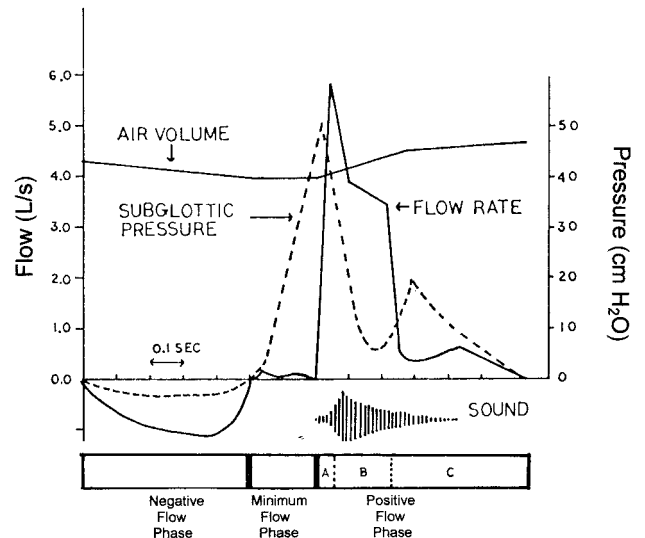

Fig. 1. Flow and pressure changes during a cough maneuver. (From Reference 2, with permission).

the glottis supports a rapid inspiratory airflow. The inspiratory phase is marked by a period of rapid inhalation, caused by contraction of the diaphragm and accessory inspiratory muscles. The volume of air spontaneously inspired may be as little as 50% of normal tidal volume or as high as 50% of vital capacity (VC).[3] Inhaling a larger volume of air produces a greater degree of lengthening in the expiratory muscles, therefore increasing the force-generation by the muscles involved in cough by improving the muscle length-tension relationship. Increasing expiratory muscle length with a greater inspired air volume generates a greater positive intrathoracic pressure and a greater expiratory flow and volume.[4] Although the greater pressure, flow, and volume are thought to improve cough function, smaller inspired volume has also been found to generate intrathoracic pressure adequate to produce an effective cough.[5]

In the compressive phase there is an almost simultaneous adduction of the glottis with the onset of expiratory-muscle contraction. The duration of this phase is approximately 0.2 s. Glottic closure is reinforced by the supraglottic ventricular folds and may also involve the epiglottis. Expiratory muscles of the rib cage and abdomen contract in a coordinated effort, compressing the alveolar gas volume. Glottic closure limits the degree of expiratory muscle shortening during contraction and increases the amount of positive intrathoracic pressure that can be generated during the compression phase. Intrathoracic pressure during the compression phase may be as great as 300 cm H_2O.

At the initiation of the expiration phase the glottis opens abruptly, within 20–40 ms. With the release of compression the central airway pressure drops to or below atmo-

spheric pressure. Pleural pressure and alveolar pressure continue to rise with expiratory-muscle contraction. The initial peak expiratory flow (PEF) may be as high as 12 L/s, and is the result of the combined effect of pressurized gas released from the alveolar space and airway gas displaced by dynamic airway compression.[4,6] The expiratory airflow in the peripheral airways depends on the volume of air initially inspired. The initial peak expiratory phase is followed by a longer expiratory phase, which lasts 0.2–0.5 s, during which airflow is in the range of 3–4 L/s.[4] Dynamic compression of the airways is the result of higher intrathoracic pressure in relation to airway gas pressure (transmural airway pressure).[5] The effect of dynamic compression in the central airways increases airflow velocity in relation to the volume of expired air per second (velocity = flow/cross-sectional area). This high linear velocity of gas in the compressed airways produces a shearing effect on the mucus lining the airway walls.[7]

Expiratory flow and dynamic compression are the primary factors that produce an effective cough. The mechanisms that affect the location of airway compression and produce maximum expiratory flow are described with the application of fluid dynamics. The location of expiratory flow limitation, called the "choke point," depends on airway pressure, the peribronchial airway pressure, and airway compliance.[8] Conditions at this point set the upper limit of flow during forced expiration or cough. Further lowering of the downstream pressure cannot increase flow through the airway. The choke point normally occurs near the tracheal carina at high lung volume in normal humans and progresses out to the peripheral airways as lung volume decreases and the airways narrow.

Dynamic compression is initiated at the trachea and mainstem bronchi at high lung volume and moves to the more peripheral airways as lung volume decreases, so the entire length of the tracheobronchial tree is "coughed."[8] The violent compression of the airway walls is thought to contribute to the formation and suspension of mucus droplets in the airway lumen.[9] During the sustained period of expiration, the airway walls may also flutter with the force of expired gas. This effect is also thought to contribute in the release of mucus droplets into the airway.

The viscosity of the mucus also affects cough efficiency. Higher mucus elasticity has a negative effect on clearance by cough but enhances mucociliary clearance.[10] In the 2-phase gas/liquid flow concept, mucus clearance is directly proportional to the depth of the mucus and inversely proportional to the mucus viscosity.[11]

The clearance of mucus from the airways during cough, by the interaction of the mucus layer with the high-linear-velocity expired gas, is described with the physical concept of 2-phase flow.[12] Three of the four 2-phase primary flow regimes (slug, annular, and mist) (Fig. 2) are thought to occur in the movement of mucus through the airways.
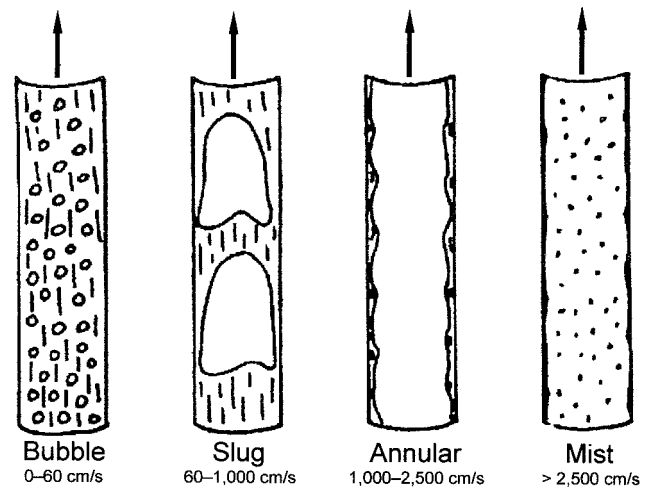

Fig 2. Two-phase current flow models. Slug, annular, and mist liquid phases are thought to be the primary means of secretion movement with high-linear-velocity gas flow during cough. (From Reference 12, with permission.)

Slug flow appears to occur with the high velocity clearance of semi-solid mucus, as evidenced by the clearance of mucus plugs. Annular flow refers to the effect of high-velocity flow through the central airway on the movement of the liquid mucus layer lining the airway. In mist flow, liquid droplets are produced and suspended as an aerosol that moves with the gas flow. The extent to which high linear gas flow affects mucus clearance by annular and mist flow during cough depends on variables including mucus viscosity and airway-wall motion. In annular flow, the increasing luminal gas velocity produces waves on the fluid surface, which create airflow resistance and shearing forces that can produce mist particles.

Mucus decreases in viscosity under high shear. This may explain the movement of mucus toward the mouth during cough-induced high shear stress, rather than distal mucus movement during the inspiratory phase. The degree of dynamic airway-wall motion may also substantially affect the interaction of high-velocity luminal airflow with the airway mucus surface layer. The extent to which each of these processes contributes to mucus clearance during cough is not well understood and probably depends on multiple interacting variables.

Pathophysiology of Neuromuscular Impaired Cough

The effectiveness of cough clearance depends on the coordinated neural sequence of phases involved in the cough maneuver and the inspiratory, expiratory, and glottic muscle functioning necessary to produce sufficient intrathoracic pressure and expiratory gas velocity. In the inspiratory phase, inhalation to VC will produce the highest intrathoracic pressure, cough volume, and cough velocity.

When neuromuscular-induced inspiratory muscle weakness limits the volume of air that can be inspired, expiratory-muscle length-tension and chest-wall recoil forces are limited,[13] which limits intrathoracic pressure and expiratory flow and volume, which limits the airway linear airflow velocity, which limits secretion clearance in the expiratory phase.

Neuromuscular diseases that cause bulbar paralysis affect the abductor and adductor muscle groups that control the glottis. Developing adductor muscle paralysis can limit the ability to close the glottis in order to generate a compression phase in the cough maneuver. The ability to generate a compression phase by closing the glottis, though beneficial in developing expiratory pressure, is not essential to produce an effective cough.[2,4] Patients with artificial airways and adequate respiratory muscle function can produce an effective cough by performing a huffing maneuver (forced exhalation through an open glottis). Paralysis of the muscles that control glottic abduction on expulsion can produce a much greater limitation in cough effectiveness. Though the inability to achieve full glottic abduction can limit the rate of inspiratory airflow, the obstruction of forced expiratory flow can severely limit cough effectiveness.[14] Intrathoracic pressure can be generated during the compression phase of cough, but the transmural airway pressure gradient can be substantially limited by severe upper-airway airflow obstruction during the expulsion phase.

Neuromuscular-induced expiratory-muscle weakness can have a substantially greater effect on cough efficiency, relative to the degree of neuromuscular weakness. Patients with mild-to-moderate expiratory-muscle weakness can experience substantial limitation in expiratory pressure.[15] The inability to generate adequate expiratory pressure (regardless of how much gas volume is inhaled) results in lower dynamic airway pressure and lower expiratory flow velocity. Patients with Duchenne muscular dystrophy or traumatic cervical-spinal-cord injury may have sufficient ventilation and yet be at risk for pulmonary congestion and acute respiratory failure associated with weak cough.[16]

DiMarco et al[17] studied the contribution of expiratory muscles to cough. They found that the interior and exterior oblique muscles and transverse abdominis muscles produced the largest contribution to airway pressure during cough stimulation. In the absence of abdominal expiratory-muscle function (as in patients with traumatic cervical spinal cord injury), cough strength is further compromised by paradoxical abdominal-wall distention during contraction of expiratory muscles of the chest wall.[18]

Chronic obstructive pulmonary disease (COPD)[19] substantially affects the mechanics of cough. One study compared esophageal pressure, airflow rate, and expired volume during a series of coughs and forced expirations in healthy subjects versus in patients with severe COPD.

Though peak pressure generated during cough was not significantly different between the groups, the peak flow and pressure resistance to flow at peak pressure was significantly lower in the COPD group.[20] This is the result of severe airway compression associated with dynamic airway pressure generated during forced expiration. For the neuromuscular patient with weak cough, a comorbidity of COPD can substantially impact an already limited cough peak flow. Though COPD can alter mucociliary function and thus increase the patient's reliance on cough to clear secretions, a greater liability for neuromuscular patients is the potential for bronchial hypersecretion and recurrent pulmonary infection.

Noninvasive respiratory-muscle aids are often applied to correct observed ventilatory impairment associated with inspiratory-muscle weakness. Cough insufficiency associated with expiratory-muscle impairment may go untreated, either because the patient does not complain of weak cough or the clinician does not perceive a need for cough support. Cough insufficiency often goes unnoticed until the occurrence of a respiratory infection that results in pulmonary congestion and acute respiratory insufficiency.

Evaluation of Cough Impairment

Cough strength depends on several contributing factors, which can be independently evaluated with various pulmonary function tests. The contribution of the inspiratory and expiratory muscle components of cough strength are commonly assessed by testing peak inspiratory pressure and peak expiratory pressure. One study compared forced vital capacity (FVC), PEF, and peak expiratory pressure in the evaluation of cough effectiveness in a group of patients with Duchenne muscular dystrophy. Peak expiratory pressure was the most sensitive predictor of transient peak flow and adequate cough strength.[21] Though respiratory-muscle strength is an important factor in the effectiveness of cough, the coordinated reflex action of the glottis in conjunction with both inspiratory and expulsion phases is necessary to produce the maximum cough flow.

FVC spirometry has been used to determine PEF as a measure of cough effectiveness (Fig. 3A). Examination of the flow-volume loops from FVC spirometry help determine the presence of neuromuscular-induced upper-airway inspiratory and expiratory flow limitation. The presence of inspiratory-flow limitation combined with intermittent irregular expiratory-flow limitation can be used to subjectively evaluate bulbar-associated glottic dysfunction (Fig. 3C).[22,23] The presence of substantial cough-flow limitation associated with obstructive airway disease can also be assessed with FVC spirometry. Expiratory cough-flow tracings have also been used to evaluate cough effectiveness. The absence of transient PEF spikes on expiratory cough-flow tracings has been associated with cough
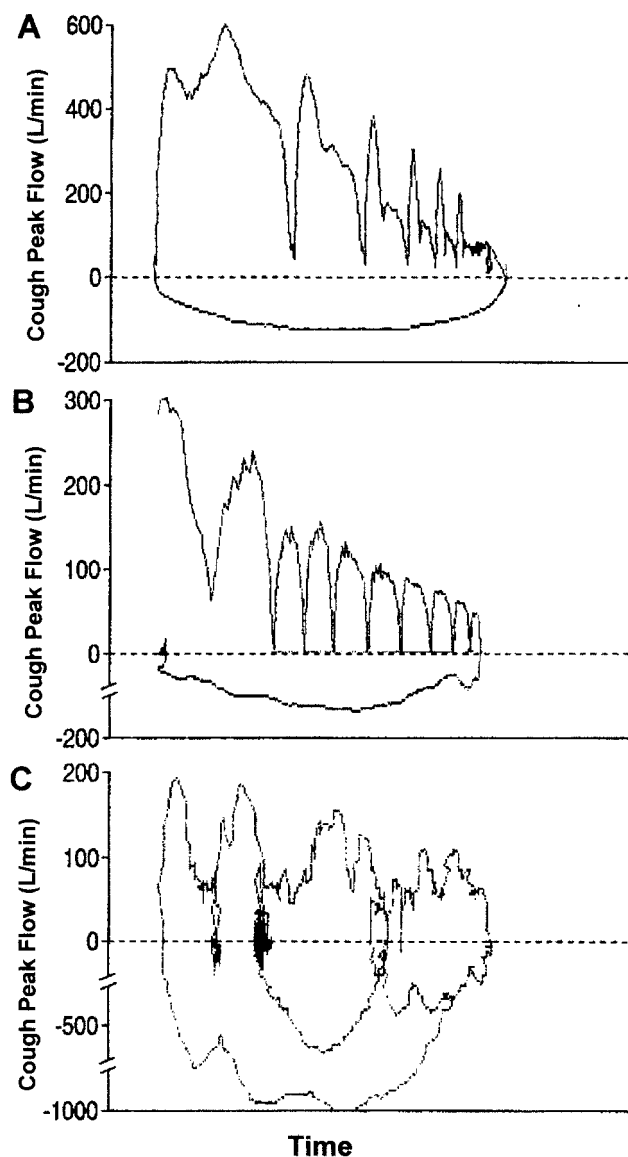
Fig. 3. Cough flow spirometry, showing (A) normal cough flow with peak cough flow spikes, (B) weakened cough flow without peak cough flow spikes, and (C) irregular cough flow associated with bulbar paralysis. (From Reference 22, with permission.)

Fig. 4. Peak-cough-flow meter with an air-cushion face mask.

limitation and mortality in motor-neuron disease (Fig. 3B).[22]

As early as 1966, peak expiratory cough flow was used as a measure of cough effectiveness.[24] The peak-expiratory-cough-flow test is administered by instructing the patient to inspire completely and cough forcibly, through either a mouthpiece or a face mask attached to a peak flow meter. Though the test is nonspecific for evaluating the separate components of cough limitation, it does provide a global measure of cough strength[25] and can be as accurately measured with a peak flow meter (Fig. 4) as with a pneumotachograph spirometer.[26] In a comparison study of peak cough flow and PEF in matched groups of normal subjects, patients with Duchenne muscular dystrophy, and patients with bulbar-onset amyotrophic lateral sclerosis (ALS),[14] peak cough flow was significantly and consistently higher than PEF in the normals and the Duchenne group. There was no significant difference in peak cough flow or PEF in the bulbar-onset ALS group.[27] This would suggest that monitoring peak cough flow and PEF could be useful in monitoring cough strength and the development of bulbar impairment in disease processes where bulbar dysfunction is predominant.

Indications for Cough-Augmentation Therapy

In a prospective study that evaluated the variables of age, extent of pre-decannulation ventilator use, VC, and peak cough flow in determining the success of extubation or decannulation of neuromuscular patients to noninvasive respiratory support, only a peak cough flow > 160 L/min predicted success in extubation and decannulation.[25] A peak expiratory cough flow of < 160 L/min has been used as a threshold for initiating cough-augmentation therapy for neuromuscular patients with cough insufficiency. Neuromuscular patients with a peak expiratory cough flow < 270 L/min are considered at risk for complications associated with respiratory infection, because their peak expiratory cough flow can fall below 160 L/min during respiratory infection.[28] A peak expiratory pressure < 60 cm H_2O or a history of repeated hospitalization for respiratory infection and an inability to clear secretions are also indications for initiating cough-augmentation therapy.[29]

Cough-Augmentation Therapies

A variety of cough-augmentation therapies or a combination of these therapies can be used to support cough
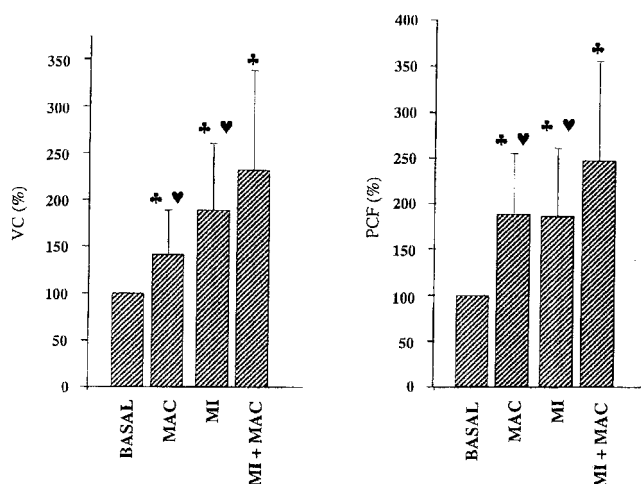
Fig. 5. Vital capacity (VC) and peak cough flow (PCF) with basal (unassisted) cough, manually assisted cough (MAC), manual insufflation (MI), and manually assisted cough plus MI. Both VC and PCF were significantly greater with MAC and MI. (From Reference 32, with permission.)

Fig. 6. Manual insufflator, consisting of a resuscitator bag, a one-way valve, a flexible tube, and a mouthpiece.

clearance, depending on the patient's needs and ability to use the various therapies. The following noninvasive cough-augmentation therapies are discussed in relation to their effectiveness and the patient's respiratory status.

Manual Cough Augmentation

Patients who have weak expiratory muscle strength but relatively well-preserved inspiratory strength can benefit from abdominal-thrust maneuvers, termed "quad cough" or "manually assisted cough," which replace or augment abdominal-muscle contraction. Quad-cough maneuvers have long been used to support cough clearance in spinal-cord-injury patients, in whom abdominal-thrust maneuvers can both prevent paradoxical abdominal-wall distention and increase intra-abdominal thoracic pressure in conjunction with the cough maneuver.[30,31] The effectiveness of this therapy depends primarily both on the caregiver's skill in applying adequate pressure and on coordinating the maneuver with the patient's voluntary cough effort. Quad-cough maneuvers can be applied to the lower abdominal area to avoid traumatizing gastrostomy tube sites, which are usually located on the upper abdominal wall. In studies that compared manually assisted cough to unassisted cough by measuring peak cough flow (Fig. 5), manually assisted cough produced significantly higher peak cough flow in various patients with neuromuscular disease and cough impairment.[19,32]

Hyperinflation Maneuvers

Patients with weak inspiratory-muscle strength can improve their spontaneous cough efforts with manual or me-chanical insufflation therapy. Manual hyperinflation can be administered by manually compressing a resuscitator bag with a one-way-valve and mouthpiece (Fig. 6), in a series of breath-stacking maneuvers, until the patient is maximally insufflated. Insufflation can also be administered mechanically, using either pressure-limited insufflation or a volume-cycled ventilator with a mouthpiece circuit that allows the patient to trigger and stack repeated ventilator breath volumes to obtain maximal insufflation.[19,33] By combining maximal insufflation with spontaneous cough maneuvers, the patient can use the stored elastic recoil energy developed with lung and chest-wall expansion to produce peak cough flow sufficient to clear secretions.

The ability to generate adequate insufflation volumes and to produce sufficient peak cough flow appears to be partly dependent on the degree of pulmonary compliance. Pulmonary compliance was evaluated by comparing the differences between maximum insufflation capacity and VC with the differences in maximum-insufflation-capacity-supported peak cough flow and unassisted peak cough flow in a large group of neuromuscular patients.[34] There was a positive correlation between the differences in maximum insufflation capacity and VC, and in the differences between maximum-insufflation-capacity-supported and spontaneous peak cough flow.[34] That study suggests that the degree of pulmonary compliance and the inspiratory phase are important in producing maximal peak cough flow and volume. Benefit from insufflation therapy also depends on having sufficient bulbar muscle strength to retain the insufflated volume. Alternatively, patients who are able to glossopharyngeal breathe (a means of inhaling by making repetitive air-gulping maneuvers) can self-insufflate enough to significantly improve peak cough flow.[35]

Fig. 7. The Emerson CoughAssist insufflator-exsufflator has manual and automatic cycle modes. Here the device is shown with an air-cushion face mask. (Courtesy of JH Emerson, Cambridge, Massachusetts.)

Functional Electrical and Magnetic Stimulation

Functional electrical stimulation can be applied with surface electrode pads on the anterior abdominal wall to produce forced expiratory-muscle contraction for cough augmentation. This technique is nearly as effective as manually assisted cough in spinal-cord-injury patients.[36,37] Forced expiratory maneuvers can also be created by applying functional magnetic stimulation with a magnetic coil in the T7 and T11 spinal area. In normal subjects, at a frequency of 25 Hz with 70–80% intensity, peak expiratory flow and pressure were comparable to maximum cough.[38] Functional electrical or magnetic stimulation of the abdominal expiratory muscles could allow the spinal-cord-injury patient independently to initiate cough maneuvers as needed. Though these techniques have been studied, there are no commercially available systems yet available.

Mechanical In-Exsufflation Therapy

Cough can be further augmented by applying combined mechanical insufflation with exsufflation, in a manual or automatic time-cycled format. Mechanical in-exsufflation is designed to produce a pressure-limited phase that insufflates the lungs, followed by a rapid reversal to negative pressure that removes the insufflated volume at an expiratory flow sufficient to clear secretions (Fig. 7). The use of mechanical in-exsufflation for secretion clearance in neuromuscular patients was first described in 1954.[39,40] In a study that evaluated mechanical in-exsufflation in the clearance of airway secretions, a mucin-thorium-dioxide suspension was instilled into the lungs of anesthetized dogs, and, after mechanical in-exsufflation, bronchograms showed nearly complete clearance in 6 min. In the same

study, mechanical in-exsufflation was equally effective in removing bronchoscopically inserted foreign bodies.[41] Mechanical in-exsufflation pressures of $+40/-40$ cm H_2O are recommended for adults using the CoughAssist device (JH Emerson, Cambridge, Massachusetts). Patients with obesity-related pulmonary restriction or increased airway resistance may require mechanical in-exsufflation pressures up to $+60/-60$ cm H_2O to produce sufficient expiratory cough flow.[42]

In a clinical-practice review of mechanical in-exsufflation for cough augmentation in a variety of pediatric neuromuscular patients, a mean mechanical in-exsufflation pressure of $+30/-30$ cm H_2O with an insufflation pressure range of $+15-40$ cm H_2O and exsufflation pressure range of -20 to -50 cm H_2O was found to be both effective and well-tolerated.[43] The duration of insufflation and exsufflation time in a mechanical in-exsufflation cycle is also a determinant in clearing secretions. The manufacturer's recommendation for insufflation time is based on low and high inspiratory-flow settings. A 3–4-s insufflation time is recommended at the lower flow setting for adults, and 1–2 s for pediatric patients. The exsufflation time is, in general, approximately half of the corresponding insufflation time. In one study, increasing the insufflation time was more effective than increasing exsufflation time in clearing secretions.[44] Mechanical in-exsufflation produced a greater peak cough flow than either manual cough or combining mechanical insufflation with manual cough, in a group of pediatric and adult neuromuscular patients.[33,45,46]

Mechanical in-exsufflation also provides an effective means of cough-augmentation maintenance for various neuromuscular patients with cough insufficiency.[43,47] In recent studies of neuromuscular patients hospitalized for pulmonary congestion associated with respiratory infection, a combination of mechanical in-exsufflation with chest physiotherapy resulted in significantly less treatment failure than chest physiotherapy alone.[48,49] Mechanical in-exsufflation is also effective in resolving postoperative pulmonary congestion.[50] The therapy is usually administered using either an air-cushion face mask or mouthpiece, but it can also be administered via artificial airway. Mechanical in-exsufflation was more effective in clearing secretions and was better tolerated than endotracheal suctioning in groups of ventilator-dependent tracheostomy patients.[51,52]

Combining Cough Therapies

Greater peak cough flow can be produced by combining insufflation therapy with assisted cough. In studies that compared peak cough flow using mechanical insufflation combined with manually assisted cough to mechanical insufflation and manually assisted cough alone, the combined therapies produced significantly higher peak cough flow than either therapy alone.[19,31-34] Bach also reported

an improvement in secretion clearance using mechanical in-exsufflation in conjunction with either abdominal thrusts or intermittent abdominal pressure ventilation synchronized with exsufflation.[33]

Limitations of Cough Augmentation

Limitations in the effectiveness of cough-augmentation therapy have been associated with 3 conditions: severe bulbar paralysis, COPD, and chest-wall restriction. In a study that evaluated the effectiveness of mechanical in-exsufflation in matched groups of patients with bulbar and nonbulbar ALS, the bulbar patients who could not generate a peak cough flow of 2.7 L/s using maximum insufflation maneuvers were also not able to generate a peak cough flow > 2.7 L/s with the aid of mechanical in-exsufflation.[53] The inability to produce the necessary peak cough flow to clear secretions is attributed to dynamic upper-airway and glottic obstruction with exsufflation.

A study that evaluated the benefit of mechanical insufflation and manually assisted cough alone and in combination, included 9 normal subjects, 8 patients with respiratory-muscle weakness, 4 patients with respiratory-muscle weakness and scoliosis, and 9 patients with COPD. Though the combined therapies produced the highest peak cough flow in the respiratory-muscle-weakness group, the respiratory-muscle-weakness-with-scoliosis group received no significant benefit from pressure-limited insufflation with manually assisted cough. The COPD group experienced significantly decreased peak flow with both manually assisted cough and combined mechanical insufflation with manually assisted cough.[19]

The ability to apply effective manually-assisted cough maneuvers may be limited by severe scoliosis, orthopedic or abdominal abnormalities, post-abdominal surgery, or the presence of indwelling abdominal or pelvic catheters. Manually-assisted coughing should not be used in patients with Greenfield filters.

Secretion Mobilization or Cough Augmentation

Understanding the pathophysiology of a patient's disease state and applying effective therapy are important in the management of respiratory disease. The decision to use secretion-mobilization and/or cough-augmentation therapy should be based on an understanding of the neuromuscular disease process. Neuromuscular respiratory insufficiency is an extrinsic lung disease in which the muscle function that usually supports ventilation, lung-volume recruitment (sighing), and cough are limited by neural and/or muscle disease. The majority of patients with neuromuscular respiratory insufficiency do not have bronchial comorbidities that limit normal mucociliary function. Manual and mechanical chest physiotherapy have been commonly used as preventive-maintenance airway-clearance therapy for pediatric patients with neuromuscular disease. There is little clinical evidence to support this therapy, unless the patient has bronchial disease that encumbers normal mucociliary function or develops pulmonary congestion associated with respiratory infection.

In a study that compared intrapulmonary percussive ventilation to manually assisted cough in a group of patients with Duchenne muscular dystrophy, mucus hypersecretion, and tracheostomy ventilation, the sputum weight collected was significantly greater from the group that underwent intrapulmonary percussive ventilation.[54] In a case series that included 3 neuromuscular patients with persistent consolidation and atelectasis that was refractory to a regimen of chest physiotherapy and manually assisted cough, intrapulmonary percussive ventilation was effective in the resolution of pulmonary congestion.[55]

The primary limitation in the secretion management of neuromuscular respiratory patients is cough clearance. Developing cough weakness in patients with neuromuscular disease will usually go unnoticed, as they have little or no need to cough, since the mucociliary system clears the normal daily mucus volume. When a respiratory infection occurs, a weak cough becomes the limiting factor in the patient's ability to maintain secretion clearance, and pulmonary congestion develops as the patient fatigues with the increased need to clear secretions. In a group of patients with Duchenne muscular dystrophy, a preventive-maintenance program of oximetry monitoring and timely cough-augmentation therapy combined with noninvasive ventilatory support was used to successfully manage respiratory infections, and the program significantly decreased the need for hospitalization.[28,56] This same noninvasive respiratory-management protocol was also successfully used with a variety of other neuromuscular patients with respiratory insufficiency—including spinal muscular atrophy, myopathy, non-Duchenne muscular dystrophy, post-polio syndrome, and ALS—with the same results.[57] In a recent study that compared mechanical in-exsufflation combined with secretion mobilization therapy to secretion mobilization therapy alone with neuromuscular patients hospitalized for pulmonary congestion associated with respiratory infection, the combined therapies significantly decreased treatment failure.[49] Mechanical in-exsufflation was also effective in the resolution of postoperative pulmonary consolidation in a patient with Duchenne muscular dystrophy who had a spinal fusion procedure.[50]

Though education and early aggressive use of airway-clearance therapy is recommended, the use of mechanical in-exsufflation is strongly supported in conjunction with oximetry monitoring in the American Thoracic Society consensus statement on the respiratory management of patients with Duchenne muscular dystrophy.[29] A global res-

piratory-management approach that monitors ventilation sufficiency, corrects for inadequate ventilation, and supports adequate cough clearance addresses the respiratory limitations associated with chronic progressive respiratory insufficiency.

Summary

The need to support airway clearance in patients with neuromuscular disease is often neglected for lack of apparent need when the patient is medically stable. The extrinsic effect of neuromuscular disease on ventilation, lung-volume recruitment, and cough is variable in both the presentation and course of the respective disease process. Though the pathophysiology of neuromuscular-induced cough insufficiency is well understood, periodic out-patient diagnostic testing to evaluate cough strength is not always done. There are several alternative means of noninvasive cough-augmentation therapy that effectively support cough clearance and, when combined with noninvasive ventilation, can significantly reduce morbidity in the respiratory management of patients with neuromuscular disease. Patients with neuromuscular disease who are hospitalized for complications of respiratory infection or for surgical procedures can be successfully supported by noninvasive secretion-mobilization and cough-augmentation therapy. A neuromuscular respiratory-management program that includes periodic evaluation of cough strength and timely initiation of effective cough-augmentation therapy can improve both the quality and duration of life for patients with respiratory insufficiency.

REFERENCES

1. Irwin RS, Boulet LP, Cloutier MM, Fuller R, Gold PM, Hoffstein V, et al. Managing cough as a defense mechanism and as a symptom. A consensus panel report of the American College of Chest Physicians. Chest 1998;114(2 Suppl Managing):133S–181S.
2. Yanagihara N, Von Leden H, Werner-Kukuk E. The physical parameters of cough: the larynx in a normal single cough. Acta Otolaryngol 1966;61(6):495–510.
3. Lawson TV, Harris RS. Assessment of the mechanical efficiency of coughing in healthy young adults. Clin Sci 1967;33(1):209–224.
4. McCool FD, Leith DE. Pathophysiology of cough. Clin Chest Med 1987;8(2):189–195.
5. McCool FD. Global physiology and pathophysiology of cough: ACCP evidence-based clinical practice guidelines. Chest 2006;129(1 Suppl):48S–53S.
6. Knudson RJ, Mead J, Knudson DE. Contribution of airway collapse to supramaximal expiratory flows. J Appl Physiol 1974;36(6):653–667.
7. Ross BB, Gramiak R, Rahn H. Physical dynamics of the cough mechanism. J Appl Physiol 1955;8(3):264–268.
8. Leith DE, Butler JP, Sneddon SL, Brain JD. Cough. In: Macklem PT, Mead J, editors. Section 3: The respiratory system. Bethesda: American Physiological Society; 1986: 315–336.
9. Leith DE. Cough. In: Brain JD, Proctor DF, Reid LM, editors. Respiratory defense mechanisms. New York: Marcel Dekker; 1977: 545–592.
10. King M, Zahm JM, Pierrot D, Vaquez-Girod S, Puchelle E. The role of mucus gel viscosity, spinnability, and adhesive properties in clearance by simulated cough. Biorheology 1989;26(4):737–745.
11. King M. Role of mucus viscoelasticity in clearance by cough. Eur J Respir Dis Suppl 1987;153:165–172.
12. Leith DE. Cough. Phys Ther 1968;48(5):439–447.
13. McCool FD, Mead J. Dyspnea on immersion: mechanisms in patients with bilateral diaphragm paralysis. Am Rev Respir Dis 1989; 139(1):275–276.
14. Hadjikoutis S, Wiles CM. Respiratory complications related to bulbar dysfunction in motor neuron disease. Acta Neurol Scand 2001; 103(4):207–213.
15. Arora NS, Gal TJ. Cough dynamics during progressive expiratory muscle weakness in healthy curarized subjects. J Appl Physiol 1981; 51(2):494–498.
16. Gozal D. Pulmonary manifestations of neuromuscular disease with special reference to Duchenne muscular dystrophy and spinal muscular atrophy. Pediatr Pulmonol 2000;29(2):141–150.
17. DiMarco AF, Romaniuk JR, Kowalski KE, Supinski G. Mechanical contribution of expiratory muscles to pressure generation during spinal cord stimulation. J Appl Physiol 1999;87(4):1433–1439.
18. Estenne M, Gorini M. Action of the diaphragm during cough in tetraplegic subjects. J Appl Physiol 1992;72(3):1074–1080.
19. Sivasothy P, Brown L, Smith IE, Shneerson JM. Effect of manually assisted cough and mechanical insufflation on cough flow of normal subjects, patients with chronic obstructive pulmonary disease (COPD), and patients with respiratory muscle weakness. Thorax 2001;56(6):438–444.
20. Loudon RG, Shaw GB. Mechanics of cough in normal subjects and in patients with obstructive respiratory disease. Am Rev Respir Dis 1967;96(4):666–677.
21. Szeinberg A, Tabachnik E, Rashed N, McLaughlin FJ, England S, Bryan CA, Levison H. Cough capacity in patients with muscular dystrophy. Chest 1988;94(6):1232–1235.
22. Chaudri MB, Liu C, Hubbard R, Jefferson D, Kinnear WJ. Relationship between supramaximal flow during cough and mortality in motor neurone disease. Eur Respir J 2002;19(3):434–438.
23. Vincken W, Elleker G, Cosio MG. Detection of upper airway muscle involvement in neuromuscular disorders using the flow-volume loop. Chest 1986;90(1):52–57.
24. Leiner GC, Abramowitz S, Small MJ, Stenby VB. Cough peak flow rate. Am J Med Sci 1966;251(2):211–214.
25. Bach JR, Saporito LR. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure: a different approach to weaning. Chest 1996;110(6):1566–1571.
26. Sancho J, Servera E, Diaz J, Marin J. Comparison of peak cough flows measured by pneumotachograph and a portable peak flow meter. Am J Phys Med Rehabil 2004;83(8):608–612.
27. Suarez AA, Pessolano FA, Monteiro SG, Ferreyra G, Capria ME, Mesa L, et al. Peak flow and peak cough flow in the evaluation of expiratory muscle weakness and bulbar impairment in patients with neuromuscular disease. Am J Phys Med Rehabil 2002;81(7):506–511.
28. Bach JR, Ishikawa Y, Kim H. Prevention of pulmonary morbidity for patients with Duchenne muscular dystrophy. Chest 1997;112(4):1024–1028.
29. Finder JD, Birnkrant D, Carl J, Farber HJ, Gozal D, Iannaccone ST, et al; American Thoracic Society. Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. Am J Respir Crit Care Med 2004;170(4):456–465.

30. Braun SR, Giovannoni R. O'Connor M. Improving the cough in patients with spinal cord injury. Am J Phys Med 1984;63(1):1–10.

31. Kirby NA, Barnerias MJ, Siebens AA. An evaluation of assisted cough in quadriparetic patients. Arch Phys Med Rehabil 1966;47(11): 705–710.

32. Trebbia G, Lacombe M, Fermanian C, Falaize L, Lejaille M, Louis A, et al. Cough determinants in patients with neuromuscular disease. Respir Physiol Neurobiol 2005;146(2–3):291–300.

33. Bach JR. Mechanical insufflation-exsufflation: comparison of peak expiratory flows with manually assisted and unassisted coughing techniques. Chest 1993;104(5):1553–1562.

34. Kang SW, Kang YS, Moon JH, Yoo TW. Assisted cough and pulmonary compliance in patients with Duchenne muscular dystrophy. Yonsei Med J 2005;46(2):233–238.

35. Feigelson CI, Dickinson DG, Talner NS, Wilson JL. Glossopharyngeal breathing as an aid to the coughing mechanism in the patient with chronic poliomyelitis in a respirator. N Engl J Med 1956; 254(13):611–613.

36. Jaeger RJ, Turba RM, Yarkony GM, Roth EJ. Cough in spinal cord injured patients: comparison of three methods to produce cough. Arch Phys Med Rehabil 1993;74(12):1358–1361.

37. Taylor PN, Tromans AM, Harris KR, Swain ID. Electrical stimulation of abdominal muscles for control of blood pressure and augmentation of cough in a C3/4 level tetraplegic. Spinal Cord 2002; 40(1):34–36.

38. Lin VW, Hsieh C, Hsiao IN, Canfield J. Functional magnetic stimulation of expiratory muscles: a noninvasive and new method for restoring cough. J Appl Physiol 1998;84(4):1144–1150.

39. Barach AL, Beck GJ. Exsufflation with negative pressure; physiologic and clinical studies in poliomyelitis, bronchial asthma, pulmonary emphysema, and bronchiectasis. AMA Arch Intern Med 1954; 93(6):825–841.

40. Beck GJ, Barach AL. Value of mechanical aids in the management of a patient with poliomyelitis. Ann Intern Med 1954;40(6):1081–1094.

41. Bickerman HA. Exsufflation with negative pressure (E.W.N.P.); elimination of radiopaque material and foreign bodies from bronchi of anesthetized dogs. AMA Arch Intern Med 1954;93(5):698–704.

42. Sancho J, Servera E, Marin J, Vergara P, Belda FJ, Bach JR. Effect of lung mechanics on mechanically assisted flows and volumes. Am J Phys Med Rehabil 2004;83(9):698–703.

43. Miske LJ, Hickey EM, Kolb SM, Weiner DJ, Panitch HB. Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough. Chest 2004;125(4):1406–1412.

44. Gomez-Merino E, Sancho J, Marin J, Servera E, Blasco ML, Belda FJ, et al. Mechanical insufflation-exsufflation: pressure, volume, and flow relationships and the adequacy of the manufacturer's guidelines. Am J Phys Med Rehabil 2002;81(8):579–583.

45. Chatwin M, Ross E, Hart N, Nickol AH, Polkey MI, Simonds AK. Cough augmentation with mechanical insufflation/exsufflation in patients with neuromuscular weakness. Eur Respir J 2003;21(3):502–508.

46. Mustfa N, Aiello M, Lyall RA, Nikoletou D, Olivieri D, Leigh PN, et al. Cough augmentation in amyotrophic lateral sclerosis. Neurology 2003;61(9):1285–1287.

47. Sato K, Ishikawa Y, Ishikawa Y, Izumi T, Okabe M, Minami R. [Changes in the clinical picture of Fukuyama type. Congenital muscular dystrophy in its advanced stage: effectiveness of mechanical ventilation systems]. No To Hattatsu 2002;34(4):330–335. *article in Japanese*

48. Hanayama K, Ishikawa Y, Bach JR. Amyotrophic lateral sclerosis. Successful treatment of mucous plugging by mechanical insufflation-exsufflation. Am J Phys Med Rehabil 1997;76(4):338–339.

49. Vianello A, Corrado A, Arcaro G, Gallan F, Ori C, Minuzzo M, Bevilacqua M. Mechanical insufflation-exsufflation improves outcomes for neuromuscular disease patients with respiratory tract infections. Am J Phys Med Rehabil 2005;84(2):83–88; discussion 89–91.

50. Marchant WA, Fox R. Postoperative use of a cough-assist device in avoiding prolonged intubation. Br J Anaesth 2002;89(4):644–647.

51. Garstang SV, Kirshblum SC, Wood KE. Patient preference for in-exsufflation for secretion management with spinal cord injury. J Spinal Cord Med 2000;23(2):80–85.

52. Sancho J, Servera E, Vergara P, Marin J. Mechanical insufflation-exsufflation vs. tracheal suctioning via tracheostomy tubes for patients with amyotrophic lateral sclerosis: a pilot study. Am J Phys Med Rehabil 2003;82(10):750–753.

53. Sancho J, Servera E, Diaz J, Marin J. Efficacy of mechanical insufflation-exsufflation in medically stable patients with amyotrophic lateral sclerosis. Chest 2004;125(4):1400–1405.

54. Toussaint M, De Win H, Steens M, Soudon P. Effect of intrapulmonary percussive ventilation on mucus clearance in Duchenne muscular dystrophy patients: a preliminary report. Respir Care 2003; 48(10):940–947.

55. Birnkrant DJ, Pope JF, Lewarski J, Stegmaier J, Besunder JB. Persistent pulmonary consolidation treated with intrapulmonary percussive ventilation: a preliminary report. Pediatr Pulmonol 1996;21(4): 246–249.

56. Gomez-Merino E, Bach JR. Duchenne muscular dystrophy: prolongation of life by noninvasive ventilation and mechanically assisted coughing. Am J Phys Med Rehabil 2002;81(6):411–415.

57. Tzeng AC, Bach JR. Prevention of pulmonary morbidity for patients with neuromuscular disease. Chest 2000;118(5):1390–1396.

Discussion

Pierson:[*] Josh, this comment doesn't relate specifically to the material you just presented, but I'm not sure we're going to have an opportunity to talk about it elsewhere, since we're about to shift into critical care.

One of the things we talked about in the initial planning of this conference is what appear to be huge disparities around the country in knowledge about and availability of the modalities we've been talking about to patients who need them. Do you have any data from surveys or other sources to illustrate these disparities? For example, I've heard that among patients with ALS, only tiny fractions of them are under the care of clinicians who offer them modalities such as the in-exsufflator or noninvasive ventilation—or even know about these things.

Benditt: First of all, I'm sorry Louis Boitano couldn't be here, because he represents the people who deal with this daily. But, yes, I do have some data, and in my third and final talk tomorrow I'm going to present a little of that data. However, you are absolutely correct: there is a disparity of use of these devices around the country and around the world. There has

* David J Pierson MD FAARC, Division of Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, Washington.

been an increase in the knowledge about these, and what's interesting is that at our hospital, and I think at Massachusetts General Hospital, once the house staff start to use these things they realize how good they are, and, hopefully, in that way their value will disseminate. But, absolutely, surveys of Muscular Dystrophy Association clinics, where a lot of this care occurs, show that there is a wide range of knowledge about the various ventilator modes, cough-support, treatments, etc. And it's a problem.

Hill: I want to underline that point, that most of our acute-care hospitals have very little knowledge about cough techniques. When patients with impaired cough are admitted, unless somebody happens to have special knowledge about things like quad cough or mechanical cough-assist devices, patients end up intubated or even tracheostomized, because no one thought to assist cough.

My question has to do with ALS patients with bulbar dysfunction. We heard in Noah Lechtzin's lecture that noninvasive ventilation works pretty poorly in that subgroup of patients, and you've just shown us that the mechanical in-exsufflator doesn't work so well either. Then what can we do to help these patients?

Benditt: Probably the most difficult part of treating neuromuscular disease is the patient who has glottic dysfunction. And I have no special tricks. I don't think there's a lot that you can do noninvasively, because, as the "portal of entry" to the respiratory system, it's crucial for everything—for the cough, as I've shown you, and for maintaining the ability to use nasal and full-face-mask interfaces. One thing that you can do for them is tracheostomy, and most authors suggest that one indication for invasive ventilation is when glottic dysfunction progresses to the point where the patient can no longer tolerate it. It's a

very tough thing. I do not have any tricks.

Lechtzin: I'll comment on that, and then I have a related question. Though I'm still skeptical, our hope is that there may be a role for high-frequency-chest-wall-oscillation (the Vest). Patients tolerate the Vest better than the in-exsufflator. And the people who make the Vest claim that, because of the way it oscillates, it propels secretions proximally and up the respiratory tract. I may have pictures showing it, although I'm not sure I understand the physiology behind it. So, potentially, the Vest may be a way to help some patients to some extent. It's been my experience, with hospitalized patients with neuromuscular disease, that if I ask the respiratory therapists about mechanical in-exsufflation they look at me like I'm crazy. Have you been able to do anything to change their thinking?

Benditt: I think it's really an exposure issue. We had in-services for all the therapists in our hospital, and we repeat that about every 2 years to show them what we're doing with the neuromuscular patients. Once the therapists got onto this and started seeing it, it just spread like wildfire. We have an in-exsufflator in the clinic that we like to demonstrate for patients, and now we're finding that it's getting taken out to the intensive-care unit, and commonly being used on tracheostomized patients. So, once they pick up on it, they really start to understand what it's about and use it. I think it is an information issue, and it requires repeated in-services and teaching. They have them at Harborview and the Veterans Affairs hospital in Seattle now, and it spreads throughout.

We tell our patients to bring their equipment with them when they come in, such as their BiPAP and CoughAssist, and often the parents and the patient will teach the hospital staff how to use it. It's very helpful when a family member can spend time with them.

We've saved intubations because of that.

And it's unfortunate, but at my hospital I have a very hard time getting my fellows interested in this as a pulmonary problem. They say, "Well, the lungs are fine, so it can't be a pulmonary problem." They don't get so interested in it, but if you look at the history of pulmonary medicine, some of the biggest things that we have done with polio and spinal-cord injury relate to ventilation, not oxygenation problems, as occurs in parenchymal lung disease. So I constantly make a pitch that this is as much a part of pulmonary medicine as acute lung injury—heresy!

Brown: Every pulmonary fellow who comes to the Respiratory Acute Care Unit at Massachusetts General Hospital gets attached to an in-exsufflator during his or her rotation, just to see what it's like. You may be amused: I once attached myself to an in-exsufflator and sucked myself down to −40 cm H_2O for 50 seconds, and for the next half an hour I felt short of breath and was coughing. I think I induced interstitial pulmonary edema with the negative pressure.

**Hill:** At least you didn't try a noose, which would probably do the same thing.

Brown: The problem that you point out is exactly the same problem that we have with cuff-deflation and speech-production in people on long-term mechanical ventilation. And, generally speaking, in the community there is very little knowledge about deflating the cuff—and, indeed, a reluctance to deflate the cuff—because of fear of hypoventilation. I hope this issue of RESPIRATORY CARE helps to spread the word about cuff-deflation.

Hill: Regarding out-patients who use the mechanical in-exsufflator, I've encountered patients who, even though they have very low cough flow, have

no problem handling their secretions, because their glottic function is intact. I'm referring to patients with Duchenne muscular dystrophy and similar conditions. They put the in-exsufflator in the closet and they don't use it, because it's not of much use most of the time. Then, when they get a bronchitis and they can't handle the increased secretion load, they're in trouble, because either they forget about the in-exsufflator (this happened to me in one case when a patient died at home of a mucus plug) or they aren't comfortable with it and can't make effective use of it. So, I absolutely *insist* that they use it every day, to stay in practice. I think this is a very important point, because the in-exsufflator doesn't work as effectively if someone is unfamiliar with it.
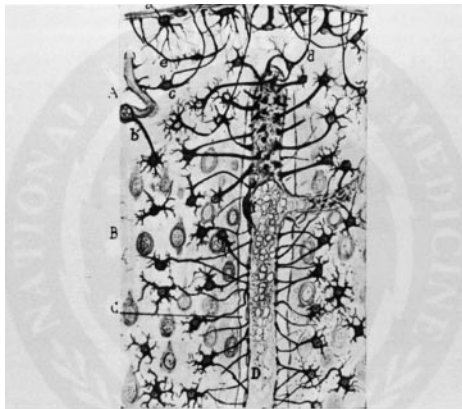
Neuroglial cells
Santiago Ramón y Cajal
Madrid, 1923
Courtesy National Library of Medicine