Appendix D

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Symptom Management During the End of Life in ALS

**Respiratory Care of The Patient with Amyotrophic Lateral Sclerosis
During the End-of-Life Period**

Respiratory failure associated with ALS is mainly due to respiratory muscle weakness. Respiratory symptoms usually develop late in the disease process and in conjunction with extremity or bulbar muscle involvement. A few patients with ALS present with respiratory symptoms initially; this is due to involvement of the phrenic motor neurons. Respiratory insufficiency can be either insidious or acute, often precipitated by infection or aspiration. Toward the terminal phase of the disease, an accelerated decrease of the pulmonary vital capacity takes place. Decreases in ventilation occur initially at night and only later, during the day. Many patients with ALS die at night, presumably as a result of an exacerbation of nocturnal hypoventilation.

Despite the frequency of respiratory failure in the patient with ALS, management of respiratory care at the end of life has not been well studied. This section summarizes recommendations based on the evidence currently available in the literature. An analysis of the current understanding of evidence-based practice recommendations also helps in identifying areas needed for future research.

WORKGROUP FINDINGS

Respiratory Function Assessment
Assessing pulmonary function and respiratory failure in patients with ALS is challenging because the ability to execute accurate spirometric testing becomes more difficult with increasing disability and disease progression. Use of a facemask rather than a mouthpiece may be helpful in obtaining spirometry, however this has not been studied scientifically. An overview of the anatomy and pathophysiology of respiratory failure is detailed in Table I. Other respiratory symptoms, other than dyspnea, are often present and may require medical attention during the end of life. Other respiratory symptoms include cough, excessive secretions, choking and laryngospasm.

Pulmonary function testing is invaluable in assessing the level of respiratory impairment, following disease progression and assessing prognosis in ALS. Fallat and colleagues evaluated comprehensive pulmonary function testing over time, in 218 patients with ALS (Fallat et al., 1987). All of their patients showed evidence of restrictive lung disease with reduction in total lung capacity (TLC), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) and maximum voluntary ventilation (MVV). The FVC averaged 80% of predicted at presentation to their clinic. They were able to follow pulmonary function tests in 103 patients, and the results showed that these patients had significant decrements in all values over time.

Black and Hyatt studied respiratory muscle function in ALS with dyspnea and near normal vital capacity (Black and Hyatt, 1971). Maximal inspiratory (MIP) and maximal expiratory (MEP) pressures were markedly reduced (34% and 47%, respectively). In these patients, reduction in maximal muscle strength correlated well with sensation of dyspnea, despite near normal vital capacity.

Nocturnal hypoventilation and sleep disordered breathing is a common problem for patients with ALS (Chokroverty, 1996; Culebras, 1996; David et al., 1997; Ferguson et al., 1996; Barthlen, 1997; Hetta, Jansson, 1997). This can occur even when respiratory muscle function is only mildly affected and daytime gas exchange remains normal. Neural output to the respiratory system normally decreases during sleep. Even mild muscle weakness coupled with the normal decreases in ventilatory drive can result in nocturnal hypoventilation and disturbed sleep architecture (Gay et al., 1991). Symptoms and signs of

nocturnal hypoventilation can manifest both at night and during the day. Nighttime symptoms include air hunger, observed apneas, orthopnea, cyanosis, restlessness and insomnia. Daytime findings include excessive sleepiness, morning headaches or drowsiness, polycythemia and pulmonary hypertension. The health care provider should be vigilant for these symptoms, which the patient may not spontaneously volunteer. Sleep studies can be very helpful in elucidating sleep disturbed breathing in these patients if doubt remains.

In addition to symptoms of hypoventilation, patients often complain of episodes of choking, cough, excess secretions and laryngospasm. Although these symptoms are known to occur, little is known of their effect on quality of life or the best treatment modalities.

Status of Knowledge of Respiratory Dysfunction During the End-of-Life Period
The recently published Practice Parameter of the American Academy of Neurology (AAN) for the care of ALS patients emphasizes respiratory care during the initial and intermediate phases of ALS, and acknowledges a paucity of information at the end of life (Miller et al., 1999). This Practice Parameter addressed whether terminal dyspnea was relieved by therapeutic intervention, and whether there was an optimal method of withdrawing noninvasive and invasive ventilation. The fear of ventilator dependency and of patients reaching a "locked-in" state, in which they are alert but unable to communicate, limited the widespread use of tracheostomy-ventilator (TV). It was thought that the use of non-invasive ventilation (e.g., NIPPV) would avoid this situation, as the technique was not thought capable of 24-hour use. However, it has become evident that patients can survive for many years with 24-hour NIPPV, particularly if techniques are used to optimally clear secretions (Bach, 1995).

One of the challenges of ventilatory support is making the decision to discontinue support during the end of life. Patients should be aware that they can discontinue NIPPV, and that severe breathlessness and anxiety can be avoided by premedication with opiates and anxiolytics. A more satisfactory alternative to abrupt discontinuation of NIPPV is to employ "terminal weaning." In terminal weaning, the settings of the ventilator are adjusted to maintain symptomatic relief but to allow gradual hypercapnia to develop; it is often done in combination with opioids and anxiolytics in order to reduce anxiety, dyspnea, pain and suffering. Careful assessment of the patient's symptoms and comfort level (frequently requiring home visits) is necessary to insure that removal of NIPPV does not actually add to anxiety and dyspnea. Very little is known about the optimum care of respiratory symptoms in the last few days of life for patients who use NIPPV.

The ALS CARE Program has generated another source of information regarding palliative care for terminal respiratory symptoms. In contrast with published data of small case series, individual case reports, or cases pertaining to terminal cancers, HIV or other disorders, the ALS Patient Care Database is a large, ongoing observational registry that allowed the study of terminal events in 1,014 ALS patients. To date, the ALS Patient Care Database represents the largest information base for ALS patients' end-of-life circumstances. The methodological strategy complements the evidence-based approach of the ALS Practice Parameter (Miller et al., 1999) by developing a planned outcome assessment using customized questionnaires. Following death, a caregiver or family member, using a standard questionnaire, provided data for each patient. In contrast with the common fear of patients and families, most patients (90.7%) died peacefully, and 62.4% died in a hospice-supported environment. Peaceful death was defined as occurring under the least amount of distress, and often related to progressive carbon dioxide narcosis, with not much pain, dyspnea or choking, as witnessed and reported by a relative or caregiver. As expected, most of the deaths (73.8%) were attributed to respiratory causes. Eight patients had stridor. Advance Directives were in place for 88.9% of patients and were followed in 96.8% of those cases. Among 67 patients who exhibited distress in the dying process, symptoms included breathing difficulties (82.1%), fear/anxiety (55.2%), pain (23.9%), insomnia (14.9%) and choking (14.9%). Preterminal oxygen was given to 52.6% of patients. Pain medications were given to 74% of patients. The results from this

study were helpful as they identify specific areas of information that are needed regarding the terminal respiratory care during the end of life. For example, no information was provided on whether the patients had been treated with non-invasive or invasive mechanical ventilation. No data were available on the use, type and dose of medications used to alleviate dyspnea. No data were available in how to treat laryngospasm, choking, mucous plugs, pain and other distressing terminal symptoms. A positive correlation between a peaceful death and income suggested that those patients with higher incomes received better end-of-life care. However, no differences were noted between different income levels with respect to the use of oxygen and pain medicine.

The Monitoring and Treatment of Respiratory Complications in ALS.

Monitoring
The respiratory specialist should be part of an interdisciplinary care team for patients with ALS because the medical care becomes more complicated as the patients experience progressive respiratory failure. Quarterly pulmonary function monitoring (every three months, as recommended by the ALS Practice Parameter [Miller et al., 1999]) is the standard recommended testing interval; however, this may change pending the individual patient's respiratory status. Pulmonary function tests provide valuable information on prognosis as well as helping to determine the timing of interventions and discussions of long-term mechanical ventilation. Furthermore, monitoring the status of pulmonary function at the end of life will help provide information regarding disease progression and the specific time course of the end of life phase.

Treatment of Respiratory Complications—Aspiration/Pneumonia
The risk of aspiration and development of pneumonia in patients with ALS is due primarily to problems with upper airway function and cough. Pharyngeal and laryngeal muscle dysfunction can lead directly to aspiration. Management of these respiratory tract symptoms include:
- Secretions and aspiration management is very common in ALS. Bulbar symptomatology is notoriously difficult to treat and is associated with a worse prognosis in terms of time to death. Oral secretions can pool in the upper respiratory tract of individuals with ALS. They can also be thick and difficult to clear because of inadequate cough and hydration. Reduction in salivary secretions is possible through the use of a number of medications and modalities (Miller et al., 1999; Blasco, Stansbury, 1996; Brodtkorb et al., 1988; Camp-Bruno et al., 1989; Newall et al., 1996; Reddihough et al., 1990). Unfortunately, they have side effects that can limit their usefulness. More recently, botulinum toxin injections into salivary glands (Giess et al., 2000), radiation therapy (Anderson et al., 2001) and even salivary gland resection have been attempted. The efficacy and utility of these techniques is currently unknown. One treatment infrequently used for laryngeal and glottic function is surgical diversion of the airway (Carter et al., 1992), a process that is invasive, dramatic and associated with standard surgical complications (Miller et al., 1999).
- Teaching of proper swallowing technique to avoid aspiration is also helpful. This involves keeping the head downward and using straws, drinking thicker rather than thin liquids, concentrating on eating during mealtime (no TV, no reading, etc.), and maintaining hydration with at least 2 quarts of water per day.
- Placement of a percutaneous gastrostomy tube (PEG) (Kasarskis, Neville, 1996; Kasarskis et al., 1999; Mathus-Vliegen et al., 1994) may help patients maintain weight and hydration. PEG placement may prevent large volume aspiration and is associated with improvement in hydration and nutritional status. Although the AAN Practice Parameter recommends placement of the tube prior to decrease of the FVC below 50%, PEG tubes may be placed in selected patients with an FVC as low as 13% (Boitano et al., 2001).

- <u>Cough function</u>, which is dependent in larger part in expiratory muscles, can be mechanically assisted when adequate bulbar function exists. Lang and Bach have proposed that cough function is adequate when the patient can generate at least 3 liters per second of peak cough flow (PCF) (Kang, Back, 2000). PCF can be routinely measured with a simple device in the clinic. When PCF drops below 180 liters per minute careful evaluation of potential interventions to improve cough function is needed. Those interventions may include teaching the caregivers how to use manually assisted cough and the Heimlich maneuver. When bulbar function is good but the patient has significant expiratory muscle weakness, an artificial cough device known as the In-exsufflator® (Emerson, Cambridge, MA) can be used. This device mimics the normal cough and has been shown to be helpful in patients with ALS and other neuromuscular diseases (Hanayama et al., 1997). As bulbar and cough function deteriorate the risk of pneumonia may increase to the point where tracheostomy will be necessary.
- <u>Choking and dysphagia</u>: There are two locations where upper airway obstruction occurs: the pharynx and the larynx. This occurs because lower motor neuron loss produces flaccidity of the pharyngeal and laryngeal muscles. As in obstructive sleep apnea, in late phase ALS, the flaccidity of pharyngeal tissue may predispose the patient to upper airway collapse and occlusion of the airway. This is more likely to happen during sleep (especially REM sleep) or when supine. The patient may begin to notice that sleeping on their back brings on a feeling of "choking." One way to help minimize this is to ask the patient to sleep on their side with the head of the bed elevated. (This feeling of choking is different from the patient complaining that they "can't catch their breath" when recumbent. A feeling of breathlessness or difficulty in taking a deep breath is usually due to diaphragmatic weakness.)

Another location where the upper airway may be obstructed is at the level of the vocal cords. Normally the vocal cords abduct during inspiration, a function provided by the posterior cricoarytenoid muscle. With the loss of bulbar lower motor neurons, this muscle weakens and the vocal cords no longer completely abduct during inspiration. This results in a smaller caliber airway. The cords themselves may contribute to a reduced airway caliber if they are inflamed or edematous from smoking, gastroesophogeal reflux disease (GERD), or allergies. Patients with a small caliber airway at the level of the vocal cords may feel dyspneic or feel their breathing is labored. Others have a feeling of "strangulation" when a mucus plug passes this level. It is unclear where this mucus or phlegm originates. Some patients feel it as "post-nasal drip" whereas in other patients it may be bronchial secretions. In either case, the mucus sits within the vestibule or on the cords and produces symptoms of airway obstruction or the sense of an inability to clear the throat. Patients with low respiratory muscle forces (maximum inspiratory pressures MIP and/or maximum expiratory pressures MEP) will complain of difficulty breathing due to upper airway obstruction at the level of the vocal cords since they cannot generate sufficient cough to clear the mucus from their airway.

Treatment of this mucus accumulation in the upper airway can be done using standard approaches to respiratory management; in addition, an evaluation by an otolaryngologist may prove helpful, and beta blockers may help, presumably by reducing pulmonary mucous production (Newall et al., 1996). If the patient has symptoms of GERD, the patient may benefit from proton pump inhibitors such as omeprazole. As described in the Practice Parameter, chest physical therapy, postural drainage and mechanical insufflation-exsufflation may be helpful in reducing upper airway secretions (Miller et al., 1999). Guaifenesin may thin the mucoid secretions (but it has never been shown to be effective in controlled trials). Very late in the disease, anticholinergic medications such as hyoscine have been recommended to dry up the airway and prevent "death rattle"(Saunders, Baines, 1989).

- Laryngospasm is an uncommon but frightening symptom that sometimes occurs in patients with ALS and can last for seconds to minutes. It is characterized by the sudden onset of stridorous inspiration caused by forceful adduction of the vocal cords. The forceful adduction of the cords is part of a group of reflexes that normally act to prevent aspiration of food or liquid into the lungs. In ALS patients, it may occur without provocation during the day, it may be precipitated by eating or drinking, or it may wake the patient from sleep. Patients have been treated with omeprazole with a marked improvement in the incidence or severity of the stridorous inspirations. In these patients, the stimulus for the stridor can be presumed to be acid reflux onto or near the larynx (Toohill et al., 1997). Sometimes the addition of small doses of diazepam or sublingual lorezepam relieves this symptom.

Predicting Ventilatory Failure

Predictive Signs, Symptoms and Laboratory Tests During Disease Progression
Progressive inspiratory muscle weakness in ALS inevitably leads to carbon dioxide retention and hypercarbic respiratory failure leading to the most common cause of death in patients with ALS. Predicting when respiratory failure will occur in the patient with ALS is important in order to plan appropriate clinical interventions and to help patients and their families address crucial decisions concerning long-term mechanical ventilation and end-of-life issues. (Discussion regarding discontinuing ventilatory support is described in detail in Appendix C: Ethics, Communication and Decision Making, and therefore not addressed here.)

Unfortunately, accurately predicting impending respiratory failure is a difficult task. Assessing symptoms of respiratory insufficiency such as dyspnea and orthopnea at each clinic visit is important. Nocturnal hypoventilation often occurs prior to the onset of daytime problems; therefore, symptoms of sleep-disordered breathing such as frequent awakening, vivid nightmares, night sweats, morning headaches and daytime hypersomnolence should be explored.

Objective measurements of pulmonary function can be helpful during the early and intermediate phases of ALS, but are not entirely predictive of either impending respiratory failure or death (Fallat et al., 1987). Upright and supine vital capacity, FVC, MIP, and even transdiaphragmatic pressure measurements (Polkey et al., 1998) have been used to try to predict respiratory failure. Pulmonary function testing during the final days and weeks of a patient's life are unnecessary and may be difficult for the patient.

Predictive Signs, Symptoms and Laboratory Tests for Terminal Respiratory Failure (End of Life)
Stambler et al. (1998) looked at a number of clinical variables to predict death in ALS. They found that serum chloride was a sensitive predictor of time to death in these patients. Serum chloride levels decreased rapidly in the months before death. The authors postulate that this represents compensation for developing respiratory acidosis. Because $PaCO_2$ can be maintained until immediately prior to respiratory failure, it is rarely necessary to obtain arterial blood gases (Fallat et al., 1987).

Overview of Specific Respiratory Tests for Patients with ALS
Most authors agree that, although it is impossible to accurately predict the lifespan of any given individual with ALS, severe restrictive disease with an FVC of less than 50% should prompt careful discussions with the patient concerning medical interventions in the event of respiratory failure (Miller et al., 1999). The frequency at which FVC measurements should be taken has not been established, but some clinics record FVC every three months (Miller et al., 1999). This measurement can easily be performed in the clinic with portable spirometry equipment.

Mechanical ventilation has been shown to be effective in both improving quality and duration of life (Lyall et al., 2001; Pinto et al., 1995; Cazzolli, Oppenheimer, 1996; Aboussouan et al., 1997; Kleopas et al., 1999). Currently, there are two major therapeutic options available for patients with ALS who have respiratory failure:

- noninvasive positive pressure ventilation (NIPPV) using a nasal mask and a positive pressure generator generally of the pressure support type, and
- tracheostomy with ventilator (TV) utilizing a tracheostomy and a standard, usually volume cycled, ventilator.

NIPPV has been shown to decrease the symptom of dyspnea (Lyall et al., 2001; Cazzolli, Oppenheimer 1996) and improve quality of life (Lyall et al., 2001) and may lengthen survival (Pinto et al., 1995; Kleopa et al., 1999). No randomized, double-blind, controlled trial of noninvasive ventilation in ALS patients has been performed, but there are several studies that lend support to the idea that life is lengthened in those patients who are able to tolerate and use this ventilatory technique (Aboussouan et al., 1997; Aboussouan et al., 2001).

Kleopa et al. (1999) retrospectively analyzed the results in 122 patients with ALS who were offered NIPPV when their FVC dropped to less than 50%. They divided their patients into those that were able to tolerate NIPPV and used it for more than 4 hours per day (Group 1), those that did not tolerate NIPPV well and used it less than 4 hours per day (Group 2) and those that refused to try NIPPV (Group 3). Mean survival was greatest in Group 1 (14.2 months) compared with Group 2 (7.0 months) and Group 3 (4.6 months). The Practice Parameters of the American Academy of Neurology suggest that all patients with ALS and respiratory symptoms or an FVC < 50% predicted should be offered the use of NIPPV (Miller et al., 1999).

NIPPV is usually initiated at night because of the high frequency of sleep-disorder breathing. Sleep studies may be helpful if symptoms are unclear and FVC > 50%, although they are not necessary to initiate treatment. As ALS disease severity progresses, patients often begin using NIPPV during the day, and many patients use this modality for 24 hours per day. Portable NIPPVs can be adapted to wheelchairs so patients can maintain limited independence.

Prior to the publication of the Practice Parameter (Miller et al., 1999), NIPPV was used in only 28% of patients with dyspnea and in 7% of patients with an FVC < 40% (Bradley et al., 2001). An attractive feature of NIPPV is that it does not require a surgical procedure and is easily removed. Unfortunately, NIPPV is only a temporary measure, and the majority of patients, sooner or later, eventually develop bulbar symptoms. Patients with ALS will be unable to continue use of NIPPV without developing aspiration pneumonia, or the device will no longer ventilate the patient effectively despite 24-hour use. At this point, invasive ventilation becomes the only option for continued survival.

Invasive ventilation (IV) involves placement of tracheostomy and usually use of a small volume-cycled home ventilator. This is clearly a life-prolonging intervention, and patients have been reported to survive for up to 20 years and more (Cazzolli, Oppenheimer, 1996). Unfortunately, invasive ventilation has no effect on the progression of the disease, and most patients will develop complete paresis of limb muscles. Approximately 10% of the patients will develop complete paresis of all muscles including the extra-ocular muscles and develop a "locked-in" syndrome in which no communication is possible. The cost of invasive ventilation to patients and families, both in financial and emotional terms, are significant (Moss et al., 1993; Moss et al., 1996; Oppenheimer, 1993). Family members provide much of the care for these patients at home and may have to relinquish employment outside the home in order to continue being the care provider. Despite this, many patients report a good quality of life while receiving mechanical ventilation with ALS (Cazzolli, Openheimer, 1996; Gelinas et al., 1998).

In a study by Sandur and Stoller (1999), complications of IV were high, including problems related to the tracheostomy such as pneumothorax, bleeding, subcutaneous emphysema, nosocomial pneumonia, tracheomalacia, tracheoarterial fistula and tracheoesophageal fistula. In this same study, complications pertaining to mechanical ventilation included pulmonary emphysema, pneumomediastinum, pneumopericardium, acute respiratory distress syndrome, venous air embolism, oxygen toxicity and systemic hemodynamic instability. The medical course for ALS patients on IV was not always smooth, but long-term survival has been the rule rather than the exception. Although medical complications, and in particular ALS-associated circulatory collapse and sudden death (Shimizu et al., 1994), accounted for the majority of death for patients on IV (Bach 1995), some IV patients simply chose to discontinue life support (Borasio, Voltz, 1998). This is reviewed below.

Most patients who undergo invasive mechanical ventilation do so in the setting of emergent hospitalization without having Advance Directives. Cazzolli and Openheimer (1996) reviewed their experience with 50 ALS patients on invasive mechanical ventilation. They found that only four (8%) of the patients had chosen tracheostomy in advance, prior to acute respiratory failure and emergent intubation. Few ALS patients have Advance Directives or living wills in place at the time that respiratory failure occurs. An instructive Advance Directive was helpful in assisting discussions of mechanical ventilation and end-of-life issues in patients with ALS (Benditt et al., 2001).

In the United States, 5% to 10 % of patients with ALS choose the option of invasive mechanical ventilation (Cazzolli, Oppenheimer, 1996; Borasio et al., 1998). The reasons why patients and family chose not to use mechanical ventilation include:

- patient expectations or fears of reduced quality of life,
- physicians not offering this as a medical option,
- the exorbitant costs of mechanical ventilation (estimates of $15,000/month), and
- unavailability of family members to assist in patient care.

The frequency of mechanical ventilation use in ALS varies worldwide from almost never (United Kingdom) to up to 48% (Japan) (Borasio et al., 1998). This appears to be due to both cultural views of ALS as well as financial and structural differences in health care systems. Fortunately, a good deal can be done to relieve some of the most troubling symptoms in patients with ALS and improve the quality of life at the end of life. Open discussion of the progression and prognosis of the disease as well as assiduous symptom management up to and including home visits can ease suffering significantly in these individuals. Dyspnea can be effectively managed both with NIPPV as well as appropriate narcotics when necessary. Home hospice services are invaluable and should be offered to these individuals. Perhaps the most important point to keep in mind is that although no cure is currently available for ALS, excellent medical care can still be provided.

Identification of Existing Gaps in Respiratory Care
Despite the quasi-absolute frequency of respiratory failure in the ALS patient, management of respiratory care at the end-of-life period has not been well-studied. Several areas still remain unexplored, particularly those relative to the use of assistive, non-invasive ventilatory supportive methods and the current availability of smaller, portable permanent ventilators. Ominous symptoms and signs of choking, aspiration, stridor and dyspnea and treatment of these symptoms have not been systematically analyzed. The effect of pain medications, particularly narcotics, on the respiratory parameters also requires a systematic analysis. The following areas in the respiratory management of the ALS should be underscored:
- Understanding the diagnosis and monitoring of respiratory failure. A number of methods have been utilized, including forced vital capacity, maximal inspiratory and expiratory pressures,

diurnal and nocturnal hypoxemia, metabolic acidosis, cough force, etc. However, despite the strong relationship between respiratory dysfunction and death in ALS, great variability in the diagnosis and treatment of respiratory failure exists.

- Due to the lack of understanding and uniformity in the diagnosis and monitoring of respiratory failure, the timing of non-invasive (NIPPV) and invasive ventilation (IV) has substantially varied from patient to patient, and has often been inadequate.
- The optimum management of symptoms in the last few days of life in patients who have chosen NIPPV is an area in which essentially nothing is known. This is a crucial area as many patients now utilize NIPPV.
- Invasive procedures, such as placement of a PEG tube or other surgical procedures have not always been performed with an understanding of the pulmonary status of the patient. This oversight has carried significant morbidity and mortality risks.
- The use of permanent ventilation has been regarded as taboo by many in the medical profession. This prejudice might affect some patients who have the desire to stay alive and have the appropriate tertiary support.
- Dysfunction of the upper airway, and events leading to aspiration pneumonia and the inadequacy of cough mechanisms, have not been specifically and systematically addressed in patients with ALS.
- Insurance support for respiratory diagnosis and management of ALS patients has not been adequate.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
1. Adhere to Practice Parameter recommendations for respiratory care for patients with ALS (Miller et al., 1999).
2. Improve physicians' sensitivity and compassion for the need of patients for respiratory assistive device, such as NIPPV and In/Exsufflator.
3. Recognize and respond to the earliest signs of respiratory compromise. Recognition of early respiratory failure may bring therapies to improve the quality of life and even prolong the life of the patient.
4. Implement NIPPV earlier rather than later in order to maximize its benefits and allow the patient to be comfortable. For many of the patients, NIPPV appears the method of choice.
5. Recognize respiratory failure and assess severity of failure prior to initiating any invasive procedure in which sedation and pain control might jeopardize the respiratory status of the patient.
6. Engage in open and thorough discussions with the patient and family that address the possible use of invasive ventilation. Scenarios might include patients with small children, who have enough family support and economic resources to see their children grow, graduate, or marry, etc.
7. Engage in early consultation with pulmonologists and respiratory therapists for comprehensive pulmonary care, prevention of infections, prevention of aspiration, immunizations, regulation of ventilator parameters and advice in the use of masks, humidifiers and exufflators, etc.

Research Recommendations
1. Conduct prospective studies to determine whether noninvasive ventilation improves quality of life and prolongs survival for patients with ALS. For example, the questions to answer are: Does NIPPV promote a better death? Does NIPPV allow the patient's goals to be met at the end of life?
2. Identify: (a) whether early ventilatory support alters prognosis; (b) the optimal timing of ventilatory intervention; and (c) better noninvasive methods of ventilatory support.
3. Study patients' wishes and feelings about living with a ventilator and identify how much the current insurance coverage interferes with a patient's wish to live with a ventilator.

4. Study methods of withdrawing both invasive and noninvasive respiratory support in ALS and how respiratory symptoms should be managed clinically (including the use of benzodiazepines, morphine, etc.).
5. Determine the best methods to detect early ventilatory failure.
6. Study the relation of progression of respiratory failure with the clinical status of the patient.
7. Study the effect of specific ALS medications (riluzole) that are being used in clinical trials on pulmonary functions and status.
8. Design prospective clinical studies aimed at analyzing the type, strength and adequacy of cough, and the effect of cough medications and enhancers.
9. Study the relationship between diurnal and nocturnal hypoventilation, the methods to alleviate them, and the significance of hypoventilation in relation to patient outcomes.
10. Study the effects of immunizations against viruses and bacteria, and the impact of these on a patient's survival.
11. Study the timing between use of NIPPV and PEG.
12. Study the use of NIPPV versus invasive ventilation in home, hospital and hospice patients.
13. Determine the effectiveness of various upper airway treatments.

Policy Recommendations
1. Current Medicare criteria for NIPPV are too strict. Lobby to have Medicare reconsider and revise the criteria allowing NIPPV. Pressure Medicare to lower the barrier for reimbursement for NIPPV and tracheostomy for at least the beginning of such treatment experience.
2. Make federal, state and private insurance companies aware of the crucial relationship between ALS and respiratory dysfunction, and the need for financial support and compensation for functional testing, NIPPV, invasive ventilators, pulmonary consultations, treatments and immunizations.
3. Make the NIH, nonprofit and for-profit organizations aware of the significant gaps between current practice and evidence-based knowledge for respiratory dysfunction in ALS, so that they may provide more funding for additional research.
4. ALS specific palliative care education should begin early in the training of health care professionals.
5. Educate patients, families and health professionals in the use of Advance Directives, particularly in relation to NIPPV versus invasive ventilation.

REFERENCES

Aboussouan LK, Khan SU, Banerjee M, Arroliga AC, Mitsumoto H. "Objective measures of the efficacy of noninvasive positive-pressure ventilation in amyotrophic lateral sclerosis." *Muscle Nerve,* 24(3):403-409, 2001..

Aboussouan LS, Khan SU, Meeker DP, Stelmach K, Mitsumoto H. "Effect of noninvasive positive-pressure ventilation on survival in amyotrophic lateral sclerosis." *Ann Intern Med.,*127:450-453, 1997.

Albert SM, Murphy PL, Del Bene ML, Rowland LP. "Prospective study of palliative care in ALS: choice, timing, outcomes." *J Neurol Sci.,*169:108-113, 1999.

Andersen PM, Gronberg H, Franzen L, Funegard U. "External radiation of the parotid glands significantly reduces drooling in patients with motor neuron disease with bulbar paresis." *J Neurol Sci,*191:111-114, 2001.

Bach JR. "Amyotrophic lateral sclerosis. Communication status and survival with ventilatory support."*Am J Phys Med Rehabil.* 72:343-349, 1993. [Published erratum appears in *Am J Phys Med Rehabil* ,73(3):218, 1994.]

Bach JR. "Amyotrophic lateral sclerosis: predictors for prolongation of life by noninvasive respiratory aids." *Arch Phys Med Rehabil.* ,76:828-832, 1995.

Barthlen GM. "Nocturnal respiratory failure as an indication of noninvasive ventilation in the patient with neuromuscular disease." *Respiration,*64:35-38.

Barthlen GM, Lange DJ. "Unexpectedly severe sleep and respiratory pathology in patients with amyotrophic lateral sclerosis." *Eur J Neurol.,*7:299-302, 2000.

Benditt JO, Smith TC, Tonelli MR. "Empowering the Individual with ALS at the end of life: disease-specific advanced care planning." *Muscle Nerve,*24:1706-1709, 2001.

Bernat JL, Cranford RE, Kittredge FI, Rosenberg RN. "Competent patients with advanced states of permanent paralysis have the right to forgo life-sustaining therapy." *Neurology* 43:224-225, 1993.

Black LF, Hyatt RE. "Maximal static respiratory pressures in generalized neuromuscular disease." *Am Rev Respir Dis.,*103:641-650, 1971.

Blasco PlA, Stansbury JCK. "Glycopyrrolate treatment of chronic drooling." *Arch Pediatr Adolesc Med.,*150:932-935, 1996.

Boitano LJ, Jordan T, Benditt JO. "Noninvasive ventilation allows gastrostomy tube placement in patients with advanced ALS." *Neurology,*56:413-414, 2001.

Borasio GD, Gelinas DF, Yanagisawa N. "Mechanical ventilation in amyotrophic lateral sclerosis: a cross- cultural perspective." *J Neurol.,*245:S7-12; discussion S29, 1998.

Borasio GD, Miller RG. "Clinical characteristics and management of ALS." *Semin Neurol.,*21:155-166, 2001.

Borasio GD, Voltz R. "Palliative care in amyotrophic lateral sclerosis." *J Neurol.,*244:S11-17, 1997.

Borasio GD, Voltz R. "Discontinuation of mechanical ventilation in patients with amyotrophic lateral sclerosis." *J Neurol*, 245:717-722.

Borasio GD. "Palliative care in ALS: searching for the evidence base. Amyotroph Lateral Scler Other Motor Neuron Disord." 2 (suppl 1):S31-35, 2001.

Bradley WG, Anderson F, Bromberg M, et al. "Current Management of ALS-Comparison of the ALS CARE Database and AAN Practice Parameter." *Neurology*56:500-504,2001.

Brodtkorb E, Wyzock-Bakowska MM, Lillevold PE, Sandvik L, Saunte C, Hestnes A. "Transdermal scopolamine in drooling." *J Ment Def Res*.32:233-237, 1988.

Campo-Bruno JA, Winsberg BG, Green-Parsons AR, Abrams JP. "Efficacy of benzotropine therapy for drooling." *Dev Med Child Neurol*.31:309-319, 1989.

Carre PC, Didier AP, Tiberge YM, Arbus LJ, Leophonte PJ. "Amyotrophic lateral sclerosis presenting with sleep hypopnea syndrome." *Chest.* 93:1309-1312, 1988.

Carter GT, Johnson ER, Bonekat HW, Lieberman JS. "Laryngeal diversion in the treatment of intractable aspiration in motor neuron disease." *Arch Phys Med Rehabil.* 73:680-682, 1992.

Carter GT, Miller RG. "Comprehensive management of amyotrophic lateral sclerosis." *Phys Med Rehabil Clin N Am.* 9:271-284, viii-ix, 1998.

Cazzolli PA, Oppenheimer EA. "Home mechanical ventilation for amyotrophic lateral sclerosis: nasal compared to tracheostomy-intermittent positive pressure ventilation." *J Neurol Sci.* 139 Suppl:123-128, 1996.

Chokroverty S. "Sleep and degenerative neurologic disorders." *Neurol Clin.,*14:807-826, 1996.

Culebras A. "Sleep and neuromuscular disorders." *Neurol Clin.,*14:791-805, 1996.

David WS, Bundlie SR, Mahdavi Z. "Polysomnographic studies in amyotrophic lateral sclerosis." *J Neurol Sci.* 152 Suppl 1:S29-35, 1997.

de Carvalho M, Matias T, Coelho F, Evangelista T, Pinto A, Luis ML. "Motor neuron disease presenting with respiratory failure." *J Neurol Sci.* 139:117-122, 1996.

Fallat RJ, Norris FH, Holden D, Kandal K, Roggero PC. "Respiratory monitoring and treatment: objective treatments using non- invasive measurements." *Adv Exp Med Biol.* 209:191-200, 1987.

Ferguson KA, Strong MJ, Ahmad D, George CF. "Sleep-disordered breathing in amyotrophic lateral sclerosis." *Chest*,110:664-966, 1996.

Fromm GB, Wisdom PJ, Block AJ. "Amyotrophic lateral sclerosis presenting with respiratory failure. Diaphragmatic paralysis and dependence on mechanical ventilation in two patients." *Chest*,71:612-614, 1977.

Ganzini L, Johnston WS, McFarland BH, Tolle SW, Lee MA. "Attitudes of patients with amyotrophic lateral sclerosis and their caregivers toward assisted suicide." *N Engl J Med.,*339:967-973, 1998.

Gay PC, Westbrook PR, Daube JR, Litchy WJ, Windebank AJ, Iverson R. "Effects of alterations in pulmonary function and sleep variables on survival in patients with amyotrophic lateral sclerosis." *Mayo Clin Proc.*,66:686-694, 1991.

Gelinas DF, O'Connor P, Miller RG. "Quality of life for ventilator-dependent ALS patients and their caregivers." *J Neurol Sci.*,160:S134-136, 1998.

Giess R, Naumann M, Werner E, et al. "Injections of botulinum toxin A into the salivary glands improve sialorrhea in amyotrophic lateral sclerosis." *J Neurol Neurosurg Psychiatry*,69:121-123, 2000.

Gryfe P, Kurtz I, Gutmann M, Laiken G. "Freedom through a single switch: coping and communicating with artificial ventilation." *J Neurol Sci.*,139:132-133, 1996.

Hanayama K, Ishikawa Y, Bach JR. "Amyotrophic lateral sclerosis. Successful treatment of mucous plugging by mechanical insufflation-exsufflation." *Am J Phys Med Rehabil. ,*76:338-339, 1997.

Hetta J, Jansson I. "Sleep in patients with amyotrophic lateral sclerosis." *J Neurol.,*244:S7-9, 1997.

Hillel A, Dray T, Miller R, et al. "Presentation of ALS to the otolaryngologist/head and neck surgeon: getting to the neurologist." *Neurology*,53:S22-5;S35-36, 1999.

Hillel AD, Miller RM. "Management of bulbar symptoms in amyotrophic lateral sclerosis." *Adv Exp Med Biol.,*209:201-221, 1987.

Kang SW, Bach JR. "Maximum insufflation capacity." *Chest*,118:61-65, 2000..

Kang SW, Bach JR. "Maximum insufflation capacity: vital capacity and cough flows in neuromuscular disease." *Am J Phys Med Rehabil.*,79:222-227, 2000.

Kasarskis EJ, Neville HE. "Management of ALS: nutritional care." *Neurology*,47:S118-120, 1996.

Kasarskis EJ, Scarlata D, Hill R, Fuller C, Stambler N, Cedarbaum JM. "A retrospective study of percutaneous endoscopic gastrostomy in ALS patients during the BDNF and CNTF trials." *J Neurol Sci.*,169:118-125, 1999.

Kleopa KA, Sherman M, Neal B, Romano GJ, Heiman-Patterson T. "Bipap improves survival and rate of pulmonary function decline in patients with ALS." *J Neurol Sci.*,164:82-88, 1999.

Leith DE. "Cough." In *Lung Biology in Health and Disease: Respiratory Defense Mechanisms, Pt 2.* Brain JD, Proctor D, Reid L (eds.) New York: Marcel Dekker; 1977.

Lyall RA, Donaldson N, Fleming T, et al. "A prospective study of quality of life in ALS patients treated with noninvasive ventilation." *Neurology*,57:153-156, 2001.

Mathus-Vliegen LM, Louwerse LS, Merkus MP, Tytgat GN, Vianney de Jong JM. "Percutaneous endoscopic gastrostomy in patients with amyotrophic lateral sclerosis and impaired pulmonary function." *Gastrointest. Endosc.*, 40:463-469, 1994.

Mazzini L, Corra T, Zaccala M, Mora G, Del Piano M, Galante M. "Percutaneous endoscopic gastrostomy and enteral nutrition in amyotrophic lateral sclerosis." *J Neurol.*, 242:695-698, 1995.

Miller RG, Rosenberg JA, Gelinas DF, et al. "Practice parameter: The care of the patient with amyotrophic lateral sclerosis (An evidence-based review)." *Muscle Nerve.*, 22:1104-1108, 1999.

Miller RG, Rosenberg JA, Gelinas DF, et al. and the ALS Practice Parameters Task Force. "Practice parameter: The care of the patient with amyotrophic lateral sclerosis (an evidence-based review):Report of the Quality Standards Subcommittee of the American Academy of Neurology." *Neurology* ,52:1311-1323, 1999.

Moss AH, Casey P, Stocking CB, Roos RP, Brooks BR, Siegler M. "Home ventilation for amyotrophic lateral sclerosis patients: outcomes, costs, and patient, family, and physician attitudes." *Neurology,* 43(2):438-443, 1993.

Moss AH, Oppenheimer EA, Casey P, Cazzolli PA, Roos RP, Stocking CB, Siegler M. "Patients with amyotrophic lateral sclerosis receiving long-term mechanical ventilation. Advance care planning and outcomes." *Chest,* 110(1):249-255, 1996.

Newall AR, Orser R, Hunt M. "The control of oral secretions in bulbar ALS/MND." *J Neurol Sci.*, 139:S43-44, 1996.

Norris FH Jr, Denys EH, Ue KS. "Old and new clinical problems in amyotrophic lateral sclerosis." In *Amyotrophic Lateral Sclerosis*, Tsubaki T, Toyokura Y (eds).. Baltimore, MD: University Park Press, 1978.

Oliver D. "The quality of care and symptom control--the effects on the terminal phase of ALS/MND." *J Neurol Sci.*, 139:S134-136, 1996.

Oppenheimer EA. "Decision-making in the respiratory care of amyotrophic lateral sclerosis: should home mechanical ventilation be used?" *Palliat Med.*,7:49-64, 1993.

Pinto AC, Evangelista T, Carvalho M, Alves MA, Sales Luis ML. "Respiratory assistance with a non-invasive ventilator (Bipap) in MND/ALS patients: survival rates in a controlled trial." *J Neurol Sci.*,129:19-26, 1995.

Polkey MI, Lyall RA, Green M, Nigel Leigh P, Moxham J. "Expiratory muscle function in amyotrophic lateral sclerosis." *Am J Respir Crit Care Med.*, 158:734-741, 1998.

Reddihough D, Johnson H, Staples M, Hudson I, Exarchos H. "Use of trihexyphenidol hydrochloride to control drooling of children with cerebral palsy." *Dev Med Child Neurol.*, 32:985-989, 1990.

Saunders C, Baines M. *Living with Dying: The Management of Terminal Disease, Second Edition*. Oxford, New York: Oxford University Press, 1989.

Stambler N, Charatan M, Cedarbaum JM. "Prognostic indicators of survival in ALS. ALS CNTF Treatment Study Group." *Neurology*, 50:66-72, 1998.

Tidwell J. "Pulmonary management of the ALS patient." *J Neurosci Nurs.*, 25:337-42, 1993.

Toohill RJ, Kuhn JC. "Role of refluxed acid in pathogenesis of laryngeal disorders." *Am J Med.*, 103(5A):100s-106s, 1997.

WORKGROUP PRODUCTS

Table I: Overview of Spirometry and the Pathophysiology of Respiratory Failure in Patients with ALS

Spirometry is used to detect respiratory muscle weakness and to predict the course of respiratory failure as measured through serial measurements. The forced vital capacity (FVC) is the most commonly used measure of respiratory function in patients with ALS. It represents measurement of both inspiratory and expiratory muscle function. The maximal inspiratory (MIP) and expiratory (MEP) pressures are often reduced in patients who have dyspnea, and appear to correlate with the degree of respiratory muscle impairment. Patients with ALS develop hypoventilation secondary to respiratory muscle weakness, with subsequent respiratory acidosis and hypoxemia. Serum chloride, a metabolic indicator of the degree of respiratory acidosis, has been identified as a prognostic factor in ALS patients (Stambler et al., 1998). Levels of serum chloride below those of lower limits of normal serum chloride signal impending respiratory decompensation.

Despite the strong relationship between respiratory dysfunction and death in ALS, great variability in the diagnosis and treatment of respiratory failure exists. Moreover, little is known about the best diagnostic and therapeutic approaches for palliative pulmonary care in patients with ALS at terminal stages.

Upper Airway Muscle Dysfunction
Patients with ALS frequently develop bulbar muscle dysfunction due to motor neuron involvement in the brainstem. Dysfunction of the lips, tongue and pharyngeal and laryngeal muscles can result in an increased risk of aspiration as well as difficulty with generating adequate glottic closure for effective cough function. Swallowing may be impaired and ingesting adequate nutrition can be trying for the patient and family alike. Choking episodes are common and may even be triggered by saliva. Secretion management is a particularly difficult issue as secretions may become viscous due to inadequate hydration (Tidwell et al., 1993). Sialorrhea (drooling) is due to inadequate handling of secretions rather than the amount of secretions as in fact salivary secretions in ALS appear to be less than in normals (Miller et al., 1999). Malnutrition due to inadequate protein-calorie intake can occur and rapid weight loss should signal the clinician to carefully assess the swallowing mechanism (Kasarskis et al., 1996). Speech and swallowing are often affected and patients may require assistive technology to communicate effectively (Gryfe et al., 1996). Because of the upper airway muscle dysfunction, patients with ALS are at risk for choking episodes and aspiration. All of these different symptoms caused by respiratory muscle insufficiency are described below.

Expiratory Muscle Dysfunction
Cough is an essential airway protection reflex. Particles are expelled from the airway through a complex set of nerve and muscle responses to cough stimulation through receptors located predominantly in the upper airway (Leith, 1977). Cough receptor stimulation results in inhalation to approximately 60% of maximum vital capacity (inspiratory phase). The glottis then closes and the abdominal muscles contract resulting in markedly elevated intrathoracic pressures without airflow (compressive phase). The glottis opens shortly thereafter and gas is propelled through the airways at very high velocities resulting in airway clearance (expiratory phase). The individual with ALS may experience cough impairment in any one or all three of the stages of cough including reduction in the inspired volume due to diaphragm weakness, inability to close the glottis completely during the compressive phase due to bulbar muscle dysfunction and inability to compress and expel intrathoracic gas because of expiratory muscle weakness. Cough is not lost until substantial levels of expiratory muscle strength are lost, due to a threshold event. Maximal expiratory pressure (MEP), a commonly used clinical measure of expiratory muscle strength, does not correlate well with the presence or absence of cough generation. Inspiratory muscle strength also does not correlate well with cough generation. Endoscopic evaluation of the patients with respiratory symptoms revealed only two patients with obvious glottic dysfunction, indicating that the presence of

glottic function alone did not ensure effective cough. Some have suggested that measurement of peak cough flow (PCF) is an effective noninvasive assessment of cough function (Bach, 1993; Bach, 1995; Kang, Bach, 2000; Kang, Bach, 2000). A measured PCF of less than 160 L/m was associated with poor cough and a high risk of respiratory infection.

Inspiratory Muscle Dysfunction
ALS often affects the inspiratory muscles including the diaphragm and external intercostal muscles. This leads to a reduction in respiratory muscle strength, restrictive lung disease and ultimately carbon dioxide retention and frank respiratory failure. In a minority of cases, respiratory muscle dysfunction leading to respiratory failure may be the presenting clinical picture for the ALS patient, but usually the symptoms of respiratory muscle insufficiency such as dyspnea occur gradually over time (Fromm et al., 1977; de Carvalho et al., 1996; Carre et al., 1988; Barthlen, Lange, 2000).

Nutritional Care and Hydration in the End of Life in ALS:

INTRODUCTION

Background and Objectives
Adequate nutrition and fluids are essential not only for survival but also for healthy body function. In 25% to 30% of patients with ALS, the bulbar muscles are first affected. Eventually, the majority of the patients with ALS develop bulbar symptoms that result in progressive dysphagia and impaired food and fluid intake. This results in malnutrition due to caloric deficiency and dehydration, which increases in severity as the disease progresses, particularly during the end-of-life stages. Progressive muscle atrophy imposes increasing metabolic demands on remaining functional muscle to maintain mobility and ventilation (Kasarskis et al., 1996). Furthermore, a state of malnutrition further impairs respiratory muscle strength (Arora, Rochester, 1981) and increases the risk of immobility, aspiration, pulmonary and systemic infections and mortality. In one study, malnutrition increased the relative risk of death by 7.7-fold in ALS patients (Desport et al., 1999).

Clinically, nutritional deficiency is evidenced by significant weight loss, muscle weakness and muscle atrophy, which can lead to progressive disability and early death (Tandan, 1995). The issue with progressive nutritional compromise is related to time. As the patient becomes more disabled and unable to eat and swallow, the risk of other complications increases. Therefore, time is a critical factor in successfully managing malnutrition and dehydration in these patients.

Nutritional compromise can be treated first by improving oral intake with supplement and various techniques; however, most patients require percutaneous endoscopic gastrostomy (PEG), which carries with it risks and benefits (Desport et al., 1999). The American Academy of Neurology (AAN) Practice Parameter Subcommittee (Miller et al., 1999) has recently provided evidence-based recommendations for nutritional management, specifically using PEG. These recommendations include:
1. PEG is indicated for patients with ALS who have symptomatic dysphagia and should be considered soon after symptom onset (Guideline).
2. For optimal safety and efficacy, a PEG should be offered and placed when the patient's vital capacity (VC) or forced vital capacity (FVC) is more than 50% of predicted (Guideline).

Complications of Malnutrition
The complications of malnutrition also pose a significant risk to the patient, such as muscle atrophy and immune deficiencies.
- Muscle Atrophy: It is well known that malnutrition caused by other diseases can result in muscle atrophy and weakness, and even diaphragmatic weakness (Murciano et al., 1994). Therefore, the malnutrition occurring in ALS can likely lead to progressive muscle atrophy and weakness that are already primary issues in ALS. The loss of muscle mass in ALS also causes significant weight loss. Patients with ALS who are mobile may decrease their physical activity, which can cause secondary disuse atrophy. Although unusual, some patients with ALS lose 30% to 50% of normal body weight at a striking rate that is out of proportion to both the degree of muscle atrophy and lack of oral intake (Norris et al., 1978). This type of malnutrition is called ALS cachexia. Chronic anemia is common in these patients. Hyperalimentation does not seem to be an effective treatment for this type of malnutrition. At autopsy, loss of body fat, including unusual fat tissues such as the omentum fat, is a striking feature, suggesting that this particular weight loss may be caused by an uncontrolled systemic catabolic event (Norris et al., 1978).

- Immunocompromize: Those who are malnourished also gradually lose immunocompetence and general resistance. The risk of possible immune impairment in patients with ALS has not been well studied.

Importantly, the risk of respiratory complications also increases with decreasing pulmonary function. Therefore, timing is a critical element in achieving success in initiating a PEG early in the disease process. Ideally, PEG should take place in the middle stages of the disease, before the real end-of-life case is required. By the definition, "dysphagia requiring an enteral feeding tube" is one triggering event for initiating end-of-life discussions. Interestingly, those patients who accept the idea of a PEG early in the disease are also more likely to actually receive a PEG when needed. Those who reject the concept of having a PEG are less likely to receive a PEG when needed (Albert et al., 1999). This suggests that education and research is one factor that may play an important role in providing optimal nutritional care for patients with ALS who have a PEG.

Methods
The Practice Parameter for ALS (Miller et al., 1999) previously established treatment guidelines for use of PEG in patients with ALS. However, additional questions remain around timing, education, nutritional balance and psychosocial considerations. Specifically:
1. Should utilization of PEG be considered part of palliative care?
2. Does PEG improve quality of life in patients at the end of life? (Mazzini et al., 1995; Chio et al., 1999)
3. How should health care providers manage patients with a PEG during the end of life?
4. How should physicians care for patients who initially declined PEG, but with increasing illness severity request PEG, despite low pulmonary function?

This paper will review the current literature available to address some of these issues and recommendations will be provided on how to address these issues in future research and policy changes. In order to further evaluate the current state of practice and specifically identify areas needed for further study, a literature search was done using traditional medical literature search methods.

Published articles were identified using Medline with key words searched including: percutaneous endoscopic gastrostomy (PEG) AND ALS; nutrition AND ALS; and malnutrition AND ALS. Abstracts were reviewed and selected for inclusion based on their relevance to managing nutrition in patients with ALS. Search methods on the indication for PEG and studies of PEG prior to publication of the practice parameter were not reviewed again, and the conclusions from the Practice Parameter are reiterated herein and referred to throughout the text.

WORKGROUP FINDINGS

In patients with ALS, onset of dysphagia is common and results in serious dehydration and malnutrition. The reduction in overall calorie intake is far more profound than protein or micronutrient intake. Interestingly, the loss of lean mass (skeletal muscle) and fat is more significant in male than in female patients, suggesting that ALS differently affects males and females. Marasmus-like malnutrition is far more prevalent in patients with ALS then other types of malnutrition (Warwood, Leigh, 1998). Therefore, the diet must be managed so calorie intake is augmented rather than protein intake increased.

Management of Malnutrition in Patients with ALS
PEG
Several clinical studies report on the clinical utility of PEG specifically in patients with ALS (Mathus-Vliegen et al., 1994; Mazzini et al., 1995). Based on this evidence available to date, current clinical guidelines recommend that PEG is indicated for patients with ALS who have symptomatic dysphagia and should be considered soon after symptom onset (Miller et al., 1999). Additionally, to ensure optimal

safety and efficacy, a PEG should be offered and placed when the patient's vital capacity (VC) or forced vital capacity (FVC) is more than 50% of predicted (Miller et al., 1999).

When the Practice Parameter treatment guidelines for ALS became available, it was thought that the guidelines on the use of PEG would change the clinical role of PEG in managing the nutritional needs of the patients with ALS. Interestingly, of 2,627 patients with ALS (enrolled in the ALS Patient Care Database from Nov. 1996 to Sept. 2000—before publication of the 1999 Practice Parameter) only 174 of them received PEG. Specifically, only 42% of patients with an ALSFRSb ≤5 (moderately severe bulbar dysfunction) actually had the PEG procedure. A key determining factor for undergoing PEG was the degree of bulbar dysfunction (particularly swallowing) and the loss of arm function (dressing and hygiene) on the ALSFRS. PEG patients overall had severe dysfunction, receiving significantly more medical intervention and services from dietitians, home care nurses, and paid attendants. These results suggest that in this group of patients, those with PEG are more ill than non-PEG patients. PEG patients used more assistive devices and technological interventions such as neck support, wheelchair, suction machine, non-invasive ventilator, tracheostomy/ventilator; it is not known whether PEG patients are generally more open to technological interventions or whether the degree of functional impairment forced them to accept more interventions. In this study sample, PEG patients had a clear trend towards poorer quality of life based on the mini-SIP scale. In contrast, caregiver burden was not different between PEG and non-PEG patients.

Improving Oral Intake
Regular assessment of parameters that indicate the start of nutritional issues is important, as several steps can be taken early in the disease to minimize the impact of these issues. As shown in Table 3, there are several parameters that can be done that will help manage oral intake concerns including selecting foods that are easier to eat, working on improving swallowing strategies, and beginning oral supplements early in order to avoid malnutrition.

Impact of PEG Placement on the End of Life
Retrospective studies indicate that survival is better if PEG is performed in patients with ALS whose FVC is greater than 50%. Survival positively correlates with greater FVC as measured prior to the procedure. In ALS, to date only one retrospective study reports on the impact of PEG placement on survival: 31 patients who elected to receive PEG lived longer (first symptom to death or tracheostomy, 38 to 17 months). Patients with ALS who declined PEG survived an average of 8 months less (30 to 13 months, P < 0.03) (Mazzini, 1995). The cumulative survival was significantly greater in the PEG group at 12, 18 and 24 months after tube placement. These investigators also pointed out that patients with PEG seemed to have a better quality of life (Chio et al., 1999). However, positive impact of PEG on survival was not found in other studies (Albert et al., 2001).

Risk of PEG in Patients with Pulmonary Compromise
Patients who have an FVC below 50% of predicted and undergo PEG may develop serious pulmonary complications because pulmonary dysfunction is often asymptomatic and can rapidly worsen after the procedure. The potential problem for the procedure can be detected by comparing FVC between sitting and supine positions. If there is more than 20% drop from sitting to supine position, there may be an increased potential risk with the PEG procedure (Lechtzin et al., 2002). In this situation, a lateral decubitus position can be chosen during the procedure, but this depends on the experience of gastroenterologists or surgeons. In general, the use of medications for conscious sedation must be minimized.

It is not uncommon that patients who declined PEG before may change their mind because they become completely unable to take oral foods. Their FVCs are likely to be below 50%, and thus they have a general increased risk from the PEG procedure. Nevertheless, PEG can be safely performed in some

patients by using NIPPV such as NIV during the procedures. However, pulmonologists and gastroenterologists must work closely together to coordinate this level of care. Additional studies are needed to further assess the long-term complication and survival benefits of PEG. Gregory and colleagues (2002) reported no differences in survival after PEG in patients with FVC either above or below 50% of predicted.

Conservative Laryngectomy or Laryngeal Diversion
Conservative laryngectomy or laryngeal diversions are alternative approaches to enteral nutrition. In some patients, aspiration pneumonia may be a recurring problem. Because PEG does not prevent aspiration, in highly selected patients who suffer from recurring aspiration pneumonia and who have become anarthric, conservative laryngectomy, or laryngeal diversion can be performed (Carter et al., 1992). This procedure is only rarely performed to prevent aspiration pneumonia. A simultaneous tracheostomy is essential. Patients can continue to consume food orally for the pleasure of eating, as long as the food is largely liquid and provided in a bolus form. This procedure is recommended in the Practice Parameter as an option (Miller et al., 1999).

Food and Fluid Need During the Terminal Stages
PEG feeding should continue as long as patients can tolerate it during the course of the disease. The presence of appetite and hunger is a crucial indication for nutritional supplementation. However, it is a common observation that patients in the advanced end-of-life stages progressively lose their energy need, and in fact, lose their appetite. It is rather unusual for patients to complain of hunger and increased appetite. For those who have PEG, gastric residual before the next feeding is the best indicator of tolerability and absorption of the enteral foods. A hospice nurse or experienced health care provider can examine the residual volume. If a residual is more than 60 ml at feeding time, additional supplementation and fluid should be postponed. Surprisingly, there is no standard approach to monitoring PEG during the end of life. If there is strong wish for terminal palliative care, the use of PEG should be discontinued (Bernat et al., 1993). If dehydration is obvious, dried tongue etc., additional fluid can by provided via PEG tube.

Withdrawing Treatment
There is a point at which the duty to try to save the patient's life is exhausted. However, this point cannot be readily defined. The decision to limit treatment may depend on a balance between the burdens that the treatment imposes and the benefits that it produces.

The Unites States Supreme Court in the landmark decision in Cruzan versus the State of Missouri (1976) concluded that both competent and incompetent citizens had the constitutional right to refuse any form of medical therapy, including hydration and nutrition (Annas, 1990). The American Academy of Neurology Ethics and Humanities Subcommittee also fully agrees that the provision of hydration and nutrition is a form of medical therapy that can be refused by a competent patient (Bernat et al., 1993). The Subcommittee also gives primacy to the autonomy and rights of self-determination of competent patients, and to autonomy's ethical foundation, the doctrine of informed consent. Competent patients ultimately have the right to refuse therapies that physicians recommend for them, even if the refusal will result in death.

A prerequisite for a patient's rational decision to accept or reject life-sustaining therapy is that the physician has conveyed adequate information to the patient. Physicians have an ethical duty to compassionately and noncoercively explain to patients the prognosis and clinical course they may expect with and without life-sustaining treatment. Ethically, physicians have the duty to communicate with absolute clarity with these patients and to ascertain that the patient's decision is carefully considered and is rational under the circumstances.

Identifying Existing Gaps in Nutritional Care of Patients with ALS

After evaluation of the clinical work done to date, several areas remain unexplored specifically in the area of managing the nutritional needs of patients with ALS during the end of life. Relative to this work, the most pronounced gap lies in the knowledge and clinical evidence regarding how and when to provide nutritional and hydrational needs during the end of life. The ongoing dilemma continues for deciding when is the optimal timing for withdrawal of nutritional support or hydration as based on clinical parameters. Additional areas that are not well studied in the area of nutritional management of patients with ALS includes:

- The time course of nutritional decline, the changes in metabolic demand, and the timing for intervention are not well studied in controlled, randomized studies. Timing is an important, yet not appreciated factor in accepting PEG. There are those who accept PEG, and those who never accept PEG. When patients accept PEG, they sometimes accept it very late and the benefits are minimized. Table 4 summarizes the current state of practice and its limitations and risk in managing nutritional needs of patients with ALS.
- Understanding the reluctance to receiving PEG is not well studied. The barriers for utilization have not been explored, and therefore, cannot be specifically addressed with interventions.
- Little evidence exists regarding how to address psychosocial issues surrounding PEG placement such as: reluctance of patients to permanently change their physical appearance; or grief related to inability to ingest food by mouth.
- Conservative laryngeal diversion is rarely used and its benefits have not been investigated.
- Evidence supporting the clinical benefits of PEG in prolonging survival is based on limited, small class-II data. Additional supportive evidence demonstrating that PEG prolongs survival is needed yet ethically challenging to implement.
- A well-designed prospective study to evaluate the nutritional status in patients with ALS and the clinical benefits and assessment of clinical outcomes following PEG interventions is urgently needed.
- Additional studies are needed that better assess body mass and weight loss. Although body weight and BMI are simple and practical measurements, they do not distinguish lean mass from body fat.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
1. Further promote and encourage neurologists, primary care physicians and patients about the clinical utility of PEG, as recommended by the American Academy of Neurology Practice Parameter for management of ALS (Miller et al., 1999).
2. Initiate aggressive patient education efforts that focus on the fact that nutritional care is an essential part of ALS. The work done to date shows that patient education can impact medical choices made during the progression of illness.
3. Identify specific treatment recommendations regarding the clinical management of nutrition. This includes specific emphasis on defining parameters for withdrawing or discontinuing nutrition and hydrational support during the end of life.
4. Define an ALS weight watch program aimed at reducing or minimizing weight loss in these patients.

Research Recommendations
1. A prospective study to investigate survival benefits and quality of life benefits with PEG is needed in order to support or negate the clinical use of PEG.

2. Studies are needed to specifically identify end-of-life improvements for patients who agree to PEG and those who decline PEG.
3. Prospective studies evaluating if PEG improves quality of life with a more sensitive instrument are needed.
4. Clinical studies are needed that identify specific caloric and hydrational needs for patients with ALS during the terminal stages of the disease.
5. Clinical studies are needed to define practice procedures that will reduce the risks associated with PEG placement. For example, use of conscious sedation, decubitus position and use of NIV.
6. Studies are needed on how to optimally educate patients and health care providers about the nutritional needs with progression of ALS, and at the end of life.

Policy Recommendations

All supplemental medical equipment needed for feeding patients with ALS needs to be covered by medical insurance. This includes feeding tubes, special equipment for eating and drinking, and even the actual nutritional supplements. Current health care coverage is limited, as illustrated in Table 5.

REFERENCES

Albert SM, Murphy PL, Del Bene ML, Rowland LP. "Prospective study of palliative care in ALS: choice, timing, outcomes." *J Neurol Sci* 169(1-2):108-113, 1999.

Albert SM, Murphy PL, Del Bene ML, Mitsumoto H, Rowland LP. "Does PEG prolong life in ALS." *ALS* , 2(S2):14, 2001.

American Society of Gastroenterology. "The role of percutaneous endoscopic gastrostomy in enteral feeding. Guidelines for clinical application." *Gastrointest Endosc* , 34(S3):35S-36S,1988.

Annas, GJ. "Nancy Cruzan and the right to die." *New Engl J Med* ,323:670-673, 1990.

Arora NS, Rochester DF. "Respiratory muscle strength and maximal voluntary ventilation in undernourished patients." *Amer Rev Respir Dis* 126:5-8,1981.

Bernat JL, Cranford RE, Kittredge FI, Rosenberg RN: "Competent patients with advanced states of permanent paralysis have the right to forgo life-sustaining therapy." *Neurology*, 43:224-225, 1993.

Carpenter WH, Fonong T, Toth MJ, et al. "Total daily energy expenditure in free-living older African-Americans and Caucasians." *Am J Physiol*, 274(1 Pt 1):E96-101, 1998.

Chio A, Finocchiaro E, Meineri P, Bottacchi E, Schiffer D, and the ALS Percutaneous Endoscopic Gastrostomy Study Group. *Neurology*, 53:1123-1125, 1999.

Desport JC, Preux PM, Truong TC, Vallat JM, Sautereau D, Couratier P. "Nutritional status is a prognostic factor for survival in ALS patients." *Neurology*, 53:1059-1063, 1999.

Forbes GB, Reina JC. "Adult lean body mass declines with age." *Metabolism*, 19:653-663, 1970.

Gregory S, Siderowff A, Golaszewski A, McCluskey L. "Gastrostomy insertion in ALS patients with low vital capacity: Respiratory support and survival." *Neurology*, 58:485-487, 2002.

Harwood AM, Leigh PN. "Indicators and prevalence of malnutrition in motor neuron disease." *Eur Neurol* , 40:159-163, 1998.

Iwata M. "Reappraisal of surgical management of aspiration in Amyotrophic lateral sclerosis." In *ALS-From Charcot to the Present and into the Future*. Rose FC (ed). London, England: Smith-Gordon. 1994.

Kanda F, Fujii Y, Takahashi K, Fujita T. "Dual-energy x-ray absorptiometry in neuromuscular diseases." *Muscle Nerve*, 17:431-435, 1994.

Kasarskis EJ, S Berryman, JG Vanderleest, AR Schneider, CJ McClain. "Nutritional status of patients with amyotrophic lateral sclerosis: relation to the proximity of death." *Am J Clin Nutr*. , 63:130-137, 1996.

Lechtzin N, Wiener CM, Shade DM, Clawson L, Diette FB. "Spirometry in the supine position improves the detection of diaphragmatic weakness in patients with amyotriphic lateral sclerosis." *Chest*, 121:436-442, 2002.

Mamel JJ. "Percutaneous endoscopic gastrostomy." *Am J Gastroenterol* 84:703-710, 1988.

Mathus-Vliegen LMH, Louwerse LS, Merkus MP, Tytgat GNS, Vianney de Jong JNFP. "Percutaneous endoscopic gastrostomy in patients with amyotrophic lateral sclerosis and impaired pulmonary function." *Gastrointest Endosc*., 40: 463-469, 1994.

Mazzini L, T Corra, M Zaccala, G Mora, M Del Piano, M Galante. "Percutaneous endoscopic gastrostomy and enteral nutrition in amyotrophic lateral sclerosis." *J Neurol.,* 242:695-698, 1995.

Miller CA. "Nutritional needs and care in amyotrophic lateral sclerosis." *Topics Clin Nutr.,* 4:15-17, 1989.

Miller RG, Rosenberg JA, Gelinas DF, et al. and the ALS Practice Parameters Task Force. "Practice parameter: The care of the patient with amyotrophic lateral sclerosis (an evidence-based review)." *Neurology* 52:1311-1323, 1999.

Mitsumoto H, Chad DA, Pioro EP. *ALS*. New York, NY: Oxford Press, 1997.

Murciano D, Rigaud D, Pingleton S, Armengaud MH, Melchior JC, Aubier M. "Diaphragmatic function in severely malnourished patients with anorexia nervosa. Effects of renutrition." *Am J Respir Crit Care Med*. 150(6 Pt 1):1569-1574, 1994.

National Research Council. *Recommended Dietary Allowances, 10th ed.* Washington, DC: National Academy Press, 1989.

Poehlman ET. "Regulation of energy expenditure in aging humans." *J Am Geriat Soc.,* 41:552-559, 1993.

Sawaya A, Saltzman E, Fuss P, Young VR, Roberts SB. "Dietary energy requirements of young and older women determined by using the doubly labeled water method." *Am J Clin Nutr.,* 62:338-344, 1995.

Shimuzu T, Hatashi H, Tanabe H. "Energy metabolism of ALS patients under mechanical ventilation and tube feeding." *Rinsho Shinkeigaku* 31:255-259, 1991.

Slowie LA, Paige MS, Antel JP. "Nutritional considerations in the management of patients with amyotrophic lateral sclerosis (ALS)." *J Am Diet Assoc.,* 83:44-47, 1983.

Tandan R, Hiser JR, Krusinski PB, Poehlman ET. "Energy requirements in amyotrophic lateral sclerosis measured by the doubly labeled water methodology." *Neurology* 52 (S2):A2-A3, 1999.

Tandan R. "Differential diagnosis II: ALS-like syndromes and ALS variants." In *Amyotrophic Lateral Sclerosis: Diagnosis and Management for the Clinician*. Belsh JM, Schiffman PL (eds.) Armonk, NY: Futura. 1996.

Tandan R. "Disorders of the upper and lower motor neurons." In*Neurology in Clinical Practice, Vol.II*. Bradley WG, Daroff RB, Fenichel GM, Marsden CD (eds.). New York, New York: Butterworth-Heinemann, 1995.

Taylor HL, Jacobs DR, Schucker B, Knudsen J, Leon AS, Debacker GJ. "A questionnaire for the assessment of leisure time physical activities." *J Chronic Dis*., 31:741-755, 1978.

Warwood AM, Leigh PN. "Indicators and prevalence of malnutrition in motor neuron disease." *Eur Neurol* , 40:159-163, 1998.

BIBLIOGRAPHY AND SUPPLEMENTAL READING

Albert SM, Murphy PL, DelBene ML, Rowland LP. "A prospective study of preferences and actual treatment choices in ALS." *Neurology* 53:278-283, 1999.

Berke EM, Gardner AW, Goran MI, Poehlman ET. "Resting metabolic rate and the influence of the pretesting environment." *Am J Clin Nutr* 55:626-629, 1992.

Brooks BR. "El Escorial World Federation of Neurology criteria for the diagnosis of amyotrophic lateral sclerosis." *J Neurol Sci* ,124 (S):96-107, 1992.

Carr-Davis EM. "Nutritional maintenance in ALS." In Mitsumoto H and Norris FH Jr (eds). *Amyotrophic Lateral Sclerosis. A Comprehensive Guide To Management*. New York: Demos 1994.

Goran MI, Poehlman ET. "Total energy expenditure and energy requirements in healthy elderly persons." *Metabolism,* 41:744-753, 1992.

James WPT, Ralph A, Ferro-Luzzi A. "Energy needs of the elderly: A new approach." In *Human Nutrition. A Comprehensive Treatise. Vol 6: Nutrition, Aging and the Elderly*. HN Munro and DE Danford (eds.). New York, NY: Plenum, 1989.

Kasarskis EJ, Scarlata D, Hill R, et al. "A retrospective study of percutaneous endoscopic gastrostomy in ALS patients during the BDNF and CNTF trials." *J Neurol Sc* 169:118-125, 1999.

Mertz W, JC Tsui, JT Judd, S Reiser, J Hallfrisch, ER Morris, PD Steele, E Lashley. "What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight." *Am J Clin Nutr*.,54:291-295, 1991.

Miller RG, Anderson FA, Bradley WG, et al. "The ALS Patient Care Database: Goals, design and early results." *Neurology*, 54:53-57, 2000.

Mitsumoto H, Chad DA, Pioro EP. "Nutritional management." In *Amyotrophic Lateral Sclerosis.* New York, NY:Oxford Press, 1998.

Mitsumoto, H "Patient choices in ALS. Life-sustaining treatment versus palliative care?" *Neurology*, 53:248-249, 1999.

Nau KL. *Changes in body composition, strength and metabolism during the progression of amyotrophic lateral sclerosis*. PhD thesis, University of Michigan, Ann Arbor, MI, 1994.

Norris FH Jr, Denys EH, Ue KS. "Old and new clinical problems in amyotrophic lateral sclerosis." In Tsubaki T, Toyokura Y (eds). *Amyotrophic Lateral Sclerosis*. Baltimore, MD; University Park Press, 1978.

Park RH, Allison MC, Lang J, et al. "Randomized comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with persisting neurological dysphagia." *BMJ*304:1406-1409, 1992.

Poehlman ET, HF Viers, M Detzer. "Influence of physical activity and dietary restraint on resting energy expenditure in young non-obese females." *Can J Physiol Pharm.,* 69:320-326, 1991.

Poehlman ET, T McAuliffe, E Danforth Jr. "Effects of age and level of physical activity on plasma norepinephrine kinetics." *Am J Physiol.,* 258:E256-E262, 1990.

Poehlman ET, TL McAuliffe, DR Van Houten, E Danforth E Jr. "Influence of age and endurance training on metabolic rate and hormones in healthy men." *Am J Physiol .,* 259: E66-E72, 1990.

Poehlman ET, Toth MJ, Ades PA, Calles-Escandon J. "Gender differences in resting metabolic rate and norepinephrine kinetics in older individuals." *Eur J Clin Invest.,* 27:23-28, 1997.

Prentice AM. (ed) *The Doubly Labeled Water Method for Measuring Energy Expenditure: Technical Recommendations for the Use in Humans*. Vienna: International Atomic Energy Agency, 1990.

Sanjak M, D Paulson, R Sufit, W Reddan, D Beaulieu, L Erickson, A Shug, BR Brooks. "Physiologic and metabolic response to progressive and prolonged exercise in amyotrophic lateral sclerosis." *Neurology,* 37:1217-1220, 1987.

Schoeller DA. "How accurate is self-reported dietary energy intake?" *Nutr Rev.,* 48:373-379, 1990.

Schoeller DA. "Measurement of energy expenditure in free-living humans by using doubly labeled water." *J Nutr.,* 118: 1278-1289, 1988.

Silani V, Kasarskis EJ, Yanagisawa N. "Nutritional management in amyotrophic lateral sclerosis: a worldwide perspective." *J Neurol.,* 245 (S2):S13-S19, 1998.

Smith RA, E Gillie, J Licht. "Palliative treatment of motor neuron disease." In *Handbook of Clinical Neurology* JMBV DeJong (ed.) Amsterdam: Elsevier, 1991.

Strong MJ, Rowe A, Rankin RN: "Percutaneous gastrojejunostomy in amyotrophic lateral sclerosis." *J Neurol Sc.,* 169:128-32, 1999.

Sufit R. "Symptomatic treatment of ALS." *Neurology,* 48 (S4):S15-S22, 1997.

The ALS CNTF Treatment Study [ACTS] Phase I-II Study Group. "The amyotrophic lateral sclerosis functional rating scale. Assessment of activities of daily living in patients with amyotrophic lateral sclerosis." *Arch Neurol*., 53:141-147, 1996.

Toth MJ, Gottleib SS, Fisher ML, Poehlman ET. "Daily energy requirements in heart failure patients." *Metabolism*, 46:1294-1298, 1997.

Weir JB de V. "New methods for calculating metabolic rate with special reference to protein metabolism." *J Physiol*., 109:1-9, 1949.

World Health Organization, Food and Agriculture Organization, United Nations University. *Energy and Protein Requirements.* Geneva: World Health Organization, 1985.

Table 1: <u>Strategies for Improving Oral Intake</u>

Selecting Appropriate Foods and Altering the Food Form
It is essential to obtain a dietitian's consultation to provide patients with practical and effective advice on how they can prepare meals that will be easy and safe to swallow. Liquids are more difficult than solid foods to swallow because the transition time from the oral to pharyngeal phase when swallowing liquids is too rapid for patients with bulbar dysfunction to coordinate. However, the thicker the liquids, the slower the transition, and thus they are easier to swallow than thin liquids. Thin liquids need to be modified into gelatins, sorbet or thin soups; a gelatin additive such as "Thick-It" can also be used. Adequate liquids, ideally 6 to 8 ounces each, per day, are essential. Solid foods that are hard, dry, crumbling or have a mixed or irregular consistency (such as ice cream with nuts) should be avoided. Thus, patients and their caregiver will have to learn ways to make dry foods moist, to make hard foods softer, and to alter foods with inconsistent and irregular textures so they are smooth and consistent.

Altering the Swallowing Strategy
Body and neck position affect swallowing, and for patients with impending dysphagia, the supine position and neck hyperextension present the most danger. These positions are likely to reduce bolus control during the deglutition phase and increase aspiration. Therefore, an upright position is necessary while eating. If the patient cannot maintain an upright position, a lateral recumbent position should be used. A neck flexion maneuver upon swallowing, called a chin tuck, is often very helpful during the deglutition phase because it minimizes the upward movement of the larynx and downward movement of the epiglottis. Turning the head to one side may also produce an effect similar to the chin tuck. A speech and language pathologist can advise on the most effective swallowing strategy when swallowing is assessed using modified barium videofluorography with various textures of barium.

As a patient's condition deteriorates, the time to finish a meal progressively increases, and the amount of food that the patient can consume at one meal may decrease. Also, patients must pay greater attention to eating, so meals become an exhausting rather than a pleasurable experience. In this situation, a regular-sized meal should be divided into smaller meals or snacks that can then be consumed more frequently during the day. Patients may need to avoid talking while eating because manipulating liquids and foods in the mouth when talking may result in aspiration or choking. For patients who have a markedly hyperactive gag reflex, cooling the anterior soft palate area (not the throat) might reduce the reflex. In ALS, team-work between speech-language pathologists and dietitians usually produce the most useful suggestions for patients.

Oral supplements
When food consumption declines, adding high-calorie foods such as sugar, honey, butter, margarine or cream can increase the caloric intake. Ready-made high-calorie liquid food supplements, such as Carnation Mild or Ensure, also should be added to regular food.

Table 2: Evaluating Nutritional Status and the Need for Enteral Nutrition

_____

History
    Usual weight and percent ideal body weight   Excessive phlegm
    Weight change: duration and percent weight loss   Current diet and food form and calorie intake
    Appetite   Estimated nutritional requirement (calories, protein and liquid)
    Dysphagia severity (per patient's history)   Time required to consume a meal

Examination
    Height and weight   ALSFRS (bulbar scale)*
    Bedside oral and general examination   Hillel Scale for Swallowing (optional)
    Bedside swallowing test   Colorado Dysphagia Disability Inventory (optional)
    Modified barium videofluorography[†]

Nutritional Assessment
    Risk for malnutrition

Recommendations
    Swallowing strategy recommendation   Diet recommendations
    Discussion and education concerning enteral nutrition   Current diet
                                                Diet change
                                                Fluids
                                                 Oral supplements and thickeners

_____

*ALSFRS = ALS Functional Rating Scale (Table 1); [†]Speech-language pathologist should attend

Table 3: <u>Detecting and Assessing Caloric Dysregulation in ALS</u>

In order to prevent malnutrition, early detection of eating difficulties is important. Regular screening at clinic visits is an important part of care for these patients. This table summarizes the steps and assessments needed to detect dysphagia, assess nutritional status and determine the need for enteral nutrition. A good medical history and medical and neurological examinations, including a review of all body systems, should easily reveal dysphagia, coexisting dysarthria and perhaps pseudobulbar manifestations.

1.   Common symptoms of dysphagia:
        a.   difficulty in chewing,
        b.   jaw weakness,
        c.   fatigue from eating,
        d.   drooling,
        e.   slow eating, and
        f.   choking or coughing on liquids and food.
2.   A lower cranial nerve examination (importantly, neurogenic dysphagia usually involves the oropharyngolaryngeal component of the swallowing mechanism, rather than the esophageal component):
        a.   muscle strength testing of the masseter,
        b.   jaw opening and closure,
        c.   lip closure,
        d.   mouth opening,
        e.   ability to pucker the lips and puff the cheeks out,
        f.   soft palate movements, and
        g.   gag and jaw reflexes; the tongue should be inspected for atrophy and fasciculations.

Body Weight: Body weight at the first office visit and at routine intervals thereafter, usually every 3 months, will be the single most important examination to detect impending malnutrition in patients with ALS.

Patient Interview: Clinical Questions to Detect Dysphagia:
        1.   How long does the patient require to finish a meal?
        2.   Does the patient finish a meal because s/he feels satiated or is too tired to continue?
        3.   Does the patient cough during swallowing?
        4.   Does the patient choke while swallowing?

Table 4: Current State and Limitations in Monitoring Nutrition in Patients with ALS

1)   Exclusive Reliance on Caloric Intake from Self-Recorded Diaries, Dietary Interviews or RDA values

Self-recording of energy intake is dependent on the cooperation of subjects, and the very act of recording energy intake may actually alter eating behavior. This problem may be particularly exaggerated when a caregiver is asked to record food intake for his/her patient. Thus, recording of food intake becomes an unreliable tool on which to exclusively base guidelines for determining caloric needs in ALS patients. Several studies in normal subjects suggest a consistent under-reporting of actual caloric intake when validated against measures of total daily caloric expenditure from doubly labeled water. Our preliminary data in ALS patients shows similar under-reporting as compared to calories expended during the same time period (see above).

The current RDA divides the adult population into two age-groups: those 23 to 50 years old and those 51 years and older (National Research Council, 1989). The frequent use of the "51 and older" category is recognized as inappropriate, as diseased aging produces an increased heterogeneity in almost all physiologic measurements. Furthermore, RDA does not take into account energy recommendations for individuals who vary in physical activity or disease state. It is evident, however, that the use of a single caloric value alone is far too crude an approach and should be abandoned for medical and nutritional planning purposes. Thus, not only should caloric intake and expenditure be simultaneously measured, but these analyses should be undertaken sequentially and on multiple occasions to precisely determine caloric requirements during the disease course.

2)   Failure of These Methods to Take into Account the Diversity of ALS Patients with Respect to Body
        composition (fat and fat-free mass), Physical Activity and Disease Severity

Thermogenesis is a function of the metabolically active cell mass. Fat-free mass, which includes largely skeletal muscle, provides the largest contribution to total daily caloric expenditure (Poehlman, 1993) decreased muscle mass in ALS patients, oxygen utilization during exercise (Karpati et al., 1979), and the oxygen cost of submaximal exercise (Sanjak et al., 1987) are significantly increased. This metabolic inefficiency in ALS patients is probably further compounded by increased energy requirement due to spasticity, increased involuntary activity in working and non-working muscles (cramps and fasciculations), and the necessity for constant postural stabilization during ambulatory physical activity. Thus, energy expended during normal physical activity is likely to be increased in ALS patients as compared to matched normal controls. Increased metabolic demands imposed by muscle atrophy, and impaired respiratory muscle strength can be added to this enhanced physical activity-related expenditure. These controlling variables need to be measured and accounted for in calculating caloric requirements in ALS patients.

3)   Lack of Appropriate Age- and Gender-Matched Normal Controls

No studies have included age- and gender-matched normal controls. Caloric expenditure is lower in females than in males (Carpenter et al., 1998; Poehlman et al., 1997), and declines with normal aging (Sawaya et al., 1995). The decline in caloric expenditure in normal aging is related to decreased skeletal muscle mass (Forbes et al., 1970; Sawaya et al., 1995). Thus, results of caloric expenditure in ALS patients must be compared to those in age- and gender-matched normal controls, and presented in relation to muscle mass.

Caloric intake is traditionally measured by recording 24-hour intake by recall, estimating intake by a prospective three-day food diary, or by comparing intake against a normal population standard such as the Recommended Daily Allowance (National Research Council, 1989). Malnutrition can be identified by

body weight (using age, gender and height references), body mass index (BMI) (weight [kg]/height [m^2] or by anthropometric (skinfold thickness) criteria. Depending on the method chosen, caloric deficiency has been reported in 70 to 100% of patients by 24-hour dietary recall (Harwood, Leigh, 1998; Slowie et al., 1983), 6 to 16% of patients by BMI criteria (Desport et al., 1999; Harwood, Leigh, 1998), and in 25% of patients by triceps skinfold thickness measurement (Harwood, Leigh, 1998). Malnutrition in ALS usually correlates with weight loss and decreased triceps skinfold thickness (Slowie et al., 1983), but not with the presence of dysphagia or stage of the disease (Harwood, Leigh, 1998; Kasarskis et al., 1996).

There is considerable variation in the prevalence of malnutrition in ALS patients, even based upon caloric intake data, the most widely used method of dietary inquiry. This may simply be an artifact of measurement due to the insensitivity of methods used; the actual prevalence of caloric malnutrition in ALS patients may be 80% to 90%, even early in the disease.

Caloric expenditure can be indirectly estimated from a measure of resting metabolic rate using a factorial approach, or directly measured in free-living subjects by the doubly labeled water technique. In the indirect approach, estimates of total daily caloric expenditure are indirectly derived by a factorial approach in which resting metabolic rate and the estimated caloric expenditure from various physical activities is summed (James et al., 1989). Although early in the disease, basal energy expenditure and indirectly-derived total energy expenditure may be similar in ALS patients and age-matched normal controls, resting metabolic rate increases as muscle atrophy and disease severity progress (Kasarskis et al., 1996). However, in patients with end-stage disease supported by ventilation and tube feeding, resting metabolic rate is decreased (Shimuzu et al., 1991). From these studies, it appears that caloric needs vary with the stage and severity of disease, being normal early, increased during active disease progression, and decreased in end-stage disease. These results from preliminary studies need to be confirmed in a statistically justified sample size of ALS patients studied sequentially using appropriate methods so as to account for any effect of disease severity, and changing body composition and physical activity levels on caloric needs.

Table 5: Medicare and Commercial Insurance Enteral Feeding Guidelines

Key Points:
- Enteral formula is only reimbursed by selected insurance companies.
- For reimbursement, enteral nutrition must be the sole source or majority of nutrition, not just a supplement to oral intake.

For Medicare the patient must meet specific guidelines:
- If they are approved for enteral coverage, the formula is covered at 80% of Medicare's allowable charge (the patient would have to pick up the remaining 20% unless they have a Medicare supplemental policy).
AND
- The above is true if the patient has Medicare part B (which they have to sign up for and pay for monthly).

Medicare B coverage guidelines:

1. Patient must have a permanent non-function or disease of the structures that normally permit food to reach and to be absorbed from the small bowel (i.e. dysphagia; definition of permanent to Medicare is 90 days or three months, so if they need TF for three months or longer, they would qualify along with meeting the other guidelines).

2. The patient must require tube feedings to provide sufficient nutrients to maintain weight and strength commensurate with the patient's overall health status (i.e. see #3).

3. The patient needs to receive 20 to 35 calorie/kg or if not, supporting documentation is needed.

4. If an enteral pump is used, supporting documentation is needed.

787.2.1	ICD 9 codes Dysphagia
335.2	ALS
263.8	malnutrition
783.2	weight loss (unintentional)

Augmentative and Alternative Communication in ALS

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is principally a motor neuron disease; in most cases, only neurons affecting voluntary motor function deteriorate. As these neurons die, the muscular functions deteriorate as well.

Considered broadly, communicating verbally involves two large networks of neurons. First, a substantial amount of brain is devoted to the generation of syntactically correct language; that is, the orderly conversion of ideas into a mental flow of what will become speech. The development of a deficit in this sphere of cognition is termed aphasia. While gross deficits in this sphere are rare in ALS, careful testing has shown deficits in verbal fluency (Iwasaki et. al, 1990), word generation and naming (Strong et. al., 1999).

The second aspect of verbal communication requires the initiation of airflow from the diaphragm (respiration), generation of sound by the vocal cords (phonation), and the modification of this into understandable speech by the muscles and tissues of the oro- and nasopharynx, the mouth and the tongue (articulation and resonation). It is this, the motor aspect of speech, which is degraded and often lost in the course of ALS.

Abnormalities of the motor aspects of speech are known collectively as dysarthria. In about one quarter of ALS patients (Gubbay et. al., 1985; Li et. al., 1990; Norris et. al., 1993), the symptomatic onset of the disease begins with weakness of the muscles of speech and swallowing. In these patients, useful speech is usually lost during the course of the disease, often quite early. The remaining three quarters of ALS patients will experience the symptomatic onset of their disease in muscles of the upper or lower extremities. A high percentage of these patients will lose their ability to effectively communicate verbally at some point in their disease. A hospice study of symptom prevalence found 77% of patients with ALS to have dysarthria/dysphonia (Hicks, Corcoran, 1993). Another study found that 75% of patients with ALS were unable to speak at the time of their death (Saunders et. al., 1981).

WORKGROUP FINDINGS

Impact of Dysarthria/Anarthria on Quality of Life
Surprisingly, little has been written on the effect of the loss of the ability to communicate on the quality of life in patients with ALS. There have been no studies evaluating the effect of augmentative and alternative communication (AAC) intervention on the quality of life of individuals with ALS (Mathy et. al., 2000). Anecdotal reports suggest that effective augmentative communication can result in an improvement in the quality of life (Bach, 1993). In other studies, a high percentage of individuals with ALS expressed interest in augmentative communication or specifically requested information regarding communication aids (Gutmann, Gryfe, 1996; Silverstein et. al., 1991). This suggests that the ability to communicate is significant to quality of life. Moreover, in a study conducted at the University of Chicago, 38% of patients who were accompanied by a relative when seeing their physician indicated that they would prefer to see their physician alone, which would require the ability to communicate.

More recent studies have pointed out that quality of life is a highly individualized concept and that measures used in the past overestimate the importance of physical function (Simmons et. al., 2000; Robbins et. al., 2001). Using measures that included existential, psychological and support domains, quality of life was found not to decline as physical function deteriorated.

Current Approach to the Management of Dysarthria/Anarthria in ALS
The approach to the management of dysarthria and anarthria has changed little over the last decade.
Patients with ALS generally pass through the following stages of dysarthria (Yorkston et. al., 1993):
- Stage 1: No detectable speech disorder,
- Stage 2: Obvious speech disorder, intelligible speech,
- Stage 3: Reduction in speech intelligibility,
- Stage 4: Natural speech supplemented by augmentative techniques, and
- Stage 5: No functional speech.

The traditional approach has been to teach patients techniques that allow them to compensate for the motor deficit in the early stages of the disease. Such techniques are not specific to individuals with ALS; rather, they comprise a corpus of strategies used by individuals who have dysarthria resulting from a variety of etiologies. However, these techniques become less effective as the oral mechanism deteriorates further. At some point, it becomes necessary to consider the introduction of augmentative and alternative communication (AAC). AAC is defined by the American Speech-Language-Hearing Association (ASHA) as "an area of clinical practice that attempts to compensate (either temporarily or permanently) for the impairment and disability patterns of individuals with severe expressive communication disorders (i.e., the severely speech-language and writing impaired) (ASHA, 1991).

The introduction of AAC techniques and devices is determined by how functional or understandable the speaker is in daily communication situations (Doyle, Phillips, 2001). When a patient reaches Stage 3, it is reasonable to begin to consider AAC techniques, which will certainly be a necessity by the time the individual reaches Stage 4. AAC techniques and devices range from low-tech to high-tech (Tables 1, 2). It is important to understand that no one device or piece of technology stands alone, and those individuals who may benefit from sophisticated voice output communication aids (VOCAs) generally utilize low-tech and unaided strategies as well. Low-tech strategies include writing, alphabet or phrase boards, eye gaze boards, etc. Unaided strategies include gestures, facial expressions and yes/no responses.

Many practitioners have reported that for most patients, a combination of approaches works best because effective devices change and communication is highly influenced by environment, message and listener (Doyle, Phillips, 2001; Zeitlin et. al., 1995). Mathy et al., (2000) reported that people with ALS tend to use unassisted or low-tech methods for communicating quick wants and needs and for conversation, but they use high-tech methods for communicating detailed information, producing written products and relating stories. Consequently, while the best form of communication will certainly change over time, it is likely to change even over the course of a day. It has been suggested that the choice of the assistive device be based upon a variety of considerations. Lasker and Bedrosian (2001) promote an AAC acceptance model, which incorporates the factors of milieu, person and technology. The following considerations are all important, but the list is by no means exhaustive. Each consideration can fit into the model proposed by Lasker and Bedrosian, and the category is denoted as follows: M (milieu), P (person), T (technology).

- Level of complexity matched to level of need (P, T),
- Regressive capability (T),
- Transportability/Size/Weight (T),
- User friendly (T),
- Iconic versus alphabetic (T),
- Cost of device (T),
- Funding source (M),
- Training time needed for patient/family (M, T),
- Amount of follow up needed (T),
- Compatibility with environmental systems and/or PC (T),

- The significance of text-to-speech capability and sex-appropriate synthesized voice (T), and
- Environment of use (M).

While most of these considerations relate to milieu and/or technology, considerations related to person (i.e., time post-onset/course of disease, attitude, personality/emotional state) as well as the user's needs and skills, must be taken into account as well.

Identification of Existing Resources

Low Technology
Low-tech communication aids generally include handwriting, alphabet boards, eye-gaze boards and very simple voice output devices (i.e., devices with a very limited number of messages). These aids may be used via the technique of partner-assisted scanning, either in visual or auditory mode. Often, these aids and strategies are used in conjunction with residual speech. For example, an individual may point to a letter on an alphabet board to indicate the first letter of the word as a clue to decoding verbal speech. Context plays a significant role in this type of communication. While some low-tech devices are commercially available from companies that specialize in assistive technology (e.g., Opticommunicator® eye gaze board [Crestwood Company], MessageMate [Words+, Inc.]), clinicians have been extremely creative in their use of equipment that is commercially available for the public but intended for the non-disability market. Examples of this are Magna Doodles®, magic slates, dry-erase boards, penlights mounted to headbands for use with alphabet or phrase boards, etc.

During the late stages of ALS, physical access becomes more effortful and slow. Mathy and colleagues (2000) suggested that communication methods that involve a communication partner, such as asking yes/no questions or partner-assisted scanning, are the communication methods of choice since they are often more efficient and less fatiguing.

High Technology
As noted previously, people with ALS have generally indicated a preference for using high-tech devices for communication of detailed or lengthy information or producing written text. High-tech devices are often referred to as voice output communication aids (VOCAs), and differ from one another by various features. Generally, features can be grouped into the categories of input method, message characteristics, output and a general catchall category of "other" for miscellaneous important features.

Input method
- Direct selection – with a body part, a physical adaptation to a body part (e.g., head pointer), or a technological extension of a body part (e.g., infrared head pointer)
- Scanning – single switch, dual switch, multiple switch
- Encoding type – alphabetic, iconic, categorical, semantic compaction, Morse Code

Message characteristics
- Types of symbols
- Storage capacity
- Vocabulary expansion
- Rate enhancement

Output features
- Voice
- Print
- Visual display other than print
- Feedback

Other
- Portability
- Size/weight
- Mounting
- Physical appearance
- Protective features (carrying case, moisture guard, etc.)
- Battery life
- Warranty

Palatal Lifts
Palatal lifts are another method of improving speech that does not necessarily fall into the categories of low- or high-tech. These devices are physical prostheses that elevate the soft palate in an attempt to compensate for hypernasality. Like the techniques for compensating for motor deficits mentioned above (in the section on traditional approaches to dysarthria management), palatal lifts are only effective as long as there is some remaining muscle function. However, the evidence demonstrates that, even for a short period of time, palatal lifts can improve quality of life and significantly reduce fatigue caused by speaking (Esposito et al., 2000). By the end stages of the disease, palatal lifts are generally considered no longer functional.

Historically, one of the most significant barriers to people with ALS obtaining augmentative communication devices (ACDs) has been the issue of funding. As of January 1, 2001, Medicare policy officially changed to allow for the coverage of ACDs (termed "speech generating devices" or "SGDs" by Medicare) under the policy regarding durable medical equipment. In addition, Medicare also changed its policy regarding the waiting period for eligibility in the event of disability. The two-year waiting period was reduced to six months for individuals with ALS. These two landmark decisions have led to a significant increase in sources of funding for ACDs.

EEG-based approaches to Augmentative Communication
In the first paragraphs of this chapter, an overview of the neurology of communication was presented. A paradigm was presented in which there was a large network of neurons which generated "language," the content, and a second large network of neurons which generated "speech," the words. The preceding sections have presented techniques and devices that allow continued communication in patients with less and less motor ability to produce speech. If a patient can move a single muscle, and therefore activate a switch, speech can be produced, albeit at painfully slow rates. Steven Hawking, the physicist at Oxford stricken with ALS since his graduate school days, continues to teach, write books and offer interviews. Anarthric, wheelchair-mobile and mechanically ventilated, he is able to communicate at a rate of an average of 12 words per minute. There is however, a population of severely affected ALS patients for whom communication is even more difficult.

Although ALS is a motor neuron disease, which is said to spare the eye movements, in patients who are very severely affected or those who are kept alive on ventilators, even these movements may eventually be lost. It is for patients such as these that attempts have been made to develop systems that allow communication without any movement at all. While a number of methods have been reported on using event related potentials, such as electroencephalogram (EEG) frequency patterns or the μ-rhythm, (see Kubler et. al., 2001) it is the generation of slow cortical potentials by paralyzed patients which may hold the most promise. With this technique, a patient is trained to voluntarily change the surface electrical potential recorded from the scalp to be more positive or negative. Fluctuations of surface potential normally occur and are the basis of the EEG. In this method, however, using visual feedback of a cursor on a computer screen, the patient can learn to "direct" the surface potential. A computer interface judges

when the cursor has hit a target range, and this "hit" then constitutes a choice. For example, the first choice may divide the first half of the alphabet from the second, and so forth, in an interactive manner. These methods, however, are painfully slow; the time required to select a letter varied between 20 and 390 seconds for trained patients (Birbaumer et al., 1999). The method has also been used as a switch that requires no movement to turn on an EEG-based communication system in two patients (Kaiser et. al., 2001). It is likely that EEG methods will remain largely confined to the research setting in the near future.

Multi-Cultural Considerations
Augmentative communication for patients who are non-native speakers of English, or do not speak English at all, presents a special challenge. Writing is perhaps the most widely used low-tech strategy for communication of needs and wants. Many patients are unable to write in English, and there may not be an available interpreter if they write in their native language. Moreover, patients from some cultures may be illiterate. Another barrier is that some cultures do not view technology as necessary or acceptable. Consequently, even if high-tech devices are available that can produce speech or written text in a patient's native language, such devices may not be accepted or provided. In these instances, professionals must be prepared to use unaided communication strategies (e.g., determining a reliable yes/no response and asking questions to elicit as much information as possible). Another possibility is to develop phrase boards in the patient's native language, hopefully aided by individuals in the patient's family, to be used via eye gaze or partner-assisted scanning.

In high-tech devices, synthesized speech is most often used when the user is capable of creating a significant body of novel information. A few dedicated devices are available in languages other than English (e.g., DynaVox Spanish version). For individuals with ALS, text-to-speech technology is the most common method for producing novel information to be spoken aloud. A number of ACDs can support speech synthesizers with different languages. A list of some of the different speech synthesizers that are available, the languages they can produce, and devices that support or contain this technology can be found in Table 1.

When synthesized speech is not an option, it is possible to consider devices that utilize digitized speech, where words and phrases can be recorded in any language. Digitized devices tend to limit the ability of the user to produce novel messages since they are not capable of text-to-speech technology. However, they can provide an option for communication of basic wants and needs, since these often are able to be reduced to a finite number of concerns. Examples of devices that are capable of handling a large amount of digitized speech are shown in Table 2. Additional resources are available through the Internet and are listed in detail in Table 3.

Identification of Existing Gaps

- Patients may not have access to an SLP, particularly one with expertise in AAC.
- Primary care providers may be unaware of available technology.
    Patients with ALS are cared for in at least three types of settings. Some patients are cared for by primary care physicians or neurologists in community office settings. In these settings, it is highly variable whether the providers have much experience with methods of augmentative communication. Other patients are cared for by neurologists in university settings or other environments with access to SLPs who may or may not have some expertise in assistive technology (AT). Others still are cared for in The ALS Association or Muscular Dystrophy Association clinic settings in which access to an SLP is more or less guaranteed. Even in this last setting, however, access to an SLP with a sophisticated working knowledge of AT may not always be possible.

- SLPs do not have adequate training and preparation to handle an AAC caseload. Unfortunately, many speech-language pathologists are not trained to deliver services to the AAC population. Ratcliff and Beukelman (1995) surveyed all SLP training programs in the U.S. Eighty-two percent of the respondents reported providing at least one course in AAC, but only 58% of the facilities surveyed responded. More importantly, less than half of the students (42%) indicated they were able to carry an AAC caseload following their graduate education. Ratcliff, Beukelman also reported that as many as 87% of speech-language pathologists indicated they had worked with individuals using AAC.

    ASHA standards for eligibility for the Certificate of Clinical Competence (CCC) require the completion of 350 clock hours of clinical practica, but there are no requirements that AAC be one of the areas of practice (ASHA, 1994). Beginning in 2005, standards will require students to demonstrate specific knowledge in the area of communication modalities (including oral, manual, augmentative and alternative communication techniques and assistive technologies), but there will still be no requirement for clock hours. While ASHA has stated that treatment of individuals requiring AAC is clearly part of the scope of professional practice (ASHA, 1993), there has not yet been a concrete directive to ensure adequate training in this area.

- ASHA has several Special Interest Divisions (SIDs), one of which focuses on AAC. Membership to the SID requires payment of a fee, but not demonstration of expertise, years of experience in the area or evidence of relevant continuing education. Currently, ASHA has no requirements that members earn continuing education units (CEUs) in order to maintain their CCC. However, this is slated to change in the next few years. Additionally, most states have licensure laws that do require evidence of CEUs for renewal of a state license. Lack of funding for AAC evaluation, ACD purchase and training.

- Current documentation process for ACD funding is too lengthy and complicated. Funding remains one of the most significant barriers to acquisition of speech-language services and devices. Although Medicare now covers ACDs, many individuals are unable to pay the 20% copay required to actually get the equipment. Furthermore, Medicare does not cover many people with ALS, although this is likely to change with the passage of the Medicare Waiver Act. While Medicaid regulations in many states include coverage for ACDs, the reimbursement for evaluation in most states is low enough so as to be considered a barrier to evaluation. Third party payers have traditionally been reluctant to cover ACDs. Although insurance funding may exist for devices, there is no provision for adequate reimbursement for evaluation and training. ACDs are complex pieces of equipment that require training to use, especially for those with no prior exposure to AAC. Finally, the requirements for submission for reimbursement in some states are so restrictive that they also can be seen as a barrier to clinicians or facilities from even entering the process.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
There is a need to educate the consumer/patient that effective communication should nearly always be possible, and that it is reasonable to expect. The following recommendations describe how this can be achieved:
1. Improve content of existing educational and resource Web sites. The Web sites of ALSA, MDA, and other Web sites already include links to Augmentative Communication sites, but few have

informative "articles" to guide patients through the maze of low-tech and high-tech solutions, or how to get access to a comprehensive evaluation.

2. Create informative brochures that elucidate the technical and financial information needed to navigate this area of health care.

3. Educate health care providers about what is available.
    a. Plenary session lectures at national meetings of ASHA, the International ALS/MND Association, the ALS courses of the American Academy of Neurology (AAN), and the Caregiver Conference given annually by ALSA should include information on maintaining effective communication. Seminars should include practical information about the acquisition of ACDs (e.g., funding, billing, reimbursement, etc.).
    b. ALSA/MDA should mandate a minimal level of expertise among clinic staff in AT.
    c. ASHA should create an educational campaign to improve the level of AAC expertise among SLPs.
    d. Education of SLPs, neurologists and ALS clinical staff should include information on partner-assisted scanning and other low-tech techniques. All physician offices should have alphabet boards and sample basic eye-gaze boards. Personnel who staff the offices should understand how to use them, and how to get information in yes/no format.

4. Establish a list of certified SLPs with a minimum number of years of experience in the provision of services to the AAC population and proof of CEUs in AAC. Organizations such as ASHA's Special Interest Division on Augmentative and Alternative Communication (SID 12) can facilitate such a document.

5. Create regional centers that provide AAC evaluation, loans of devices and post-placement training of patients and families. This would help amortize the high cost of these devices across the whole community and extend the device life. In many cases, because of the rapidly lethal nature of ALS, patients die "early" in the operational life of a device. This plan would extend the life and cost effectiveness of these devices. These centers would need to be staffed by qualified SLPs.

Research Recommendations
1. Identify problems of acquisition and utilization of AAC.
2. Define the impact of inability to communicate on quality of life.
3. Define the impact of inability to communicate on interaction with health care providers.
4. Define the relationship between inability to communicate and social isolation and suffering.
5. Determine the effectiveness of AAC intervention for individuals with ALS, and its impact on quality of life.
6. Determine whether recent Medicare changes have increased AAC acquisition and use.
7. Determine the best model for AAC service delivery to individuals with ALS.
8. Determine whether AAC prevents or reduces caregiver burden and the extent of the prevention or reduction of caregiver burden.
9. Determine the effect of AAC intervention in making positive changes in the domains of functional limitation, disability and societal limitations according to the World Health Organization (WHO) framework.
10. Determine whether the recommended technology (high-tech, low-tech or combination) improves the patients' ability to communicate, and with whom and in what environment(s).

Policy Recommendations
1. Third-party payers need to provide adequate reimbursement for SLPs to evaluate and train patients who need ACDs.
2. Third-party payers other than Medicare and Medicaid, especially HMOs, need to add ACDs to their covered benefits.
3. The documentation requirements for ACD submission need to be streamlined.
4. The AAN should include communication in a future ALS Practice Parameter.

REFERENCES

American Speech-Language-Hearing Association. "Augmentative and alternative communication." *ASHA*, 33 (S 5):8, 1991.

American Speech-Language-Hearing Association. *American Speech-Language-Hearing Association Membership and Certification Handbook.* Rockville, MD, 1994.

American Speech-Language-Hearing Association. "Preferred practice patterns for the professions of speech-language pathology and audiology." *ASHA*, 35(S11):61-62, 1993.

Bach JR. "Amyotrophic lateral sclerosis. Communication status and survival with ventilatory support." *Am J Phys Med Rehabil.*, 72:343-349, 1993.

Esposito SJ, Mitsumoto H, Shanks M. "Use of palatal lift and palatal augmentation prostheses to improve dysarthria in patients with amyotrophic lateral sclerosis: a case series." *J Prosthet Dent,* 83(1):90-98,2000.

Doyle M, Phillips B. "Trends in augmentative and alternative communication use by individuals with Amyotrophic lateral sclerosis." *Augmentative and Alternative Communication.* 17 (3):167-178, 2001.

Gubbay SS, Kahana E, Zilber N, et al. "Amyotrophic lateral sclerosis. A study of its presentation and prognosis." *J Neurol.,*232:295-300, 1985.

Gutmann M. Gryfe P. "The communication continuum in ALS: Critical paths and client preferences."*Proceedings of the Seventh Biennial Conference of the International Society of Augmentative and Alternative Communication*394-395, 1996.

Hicks F, Corcoran G. "Should hospices offer respite admissions to patients with motor neuron disease?"*Palliat Med.*, 7:145-150, 1993.

Institute of Medicine *Disability in America: Toward a National Agenda for Prevention*. Washington, DC: National Academy Press, 1991.

Iwasaki Y, Kinoshita M, Ikeda K, et al. "Cognitive impairment in amyotrophic lateral sclerosis and its relation to motor disabilities." *Acta Neurol Scand.* 81:141-143, 1990.

Kaiser J, Perelmouter J, Iversen IH, et al. "Self-initiation of EEG-based communication in paralyzed patients." *Clin Neurophysiol.* 112:551-554, 2001.

Kubler A, Kotchoubey B, Kaiser J, et al. "Brain-computer communication: unlocking the locked in." *Psychol Bull* 127(3): 358-375, 2001.

Lasker JP, Bedrosian JL. "Promoting acceptance of augmentative and alternative communication by adults with acquired communication disorders." *AAC,* 17 (3):141-153, 2001.

Li TM, Alberman E, Swash M. "Clinical features and associations of 560 cases of motor neuron disease." *J Neurol Neurosurg Psychiatry*, 53:1043-1045, 1990.

Mathy P, Yorkston K, Gutmann M. "Augmentative communication for individuals with Amyotrophic lateral sclerosis." In *Augmentative And Alternative Communication In Adults With Acquired Neurologic Disorders* Beukelman D, Yorkston K, Reichle K. (eds.) Baltimore, MD: Paul H. Brookes, 2000.

Norris FH, Shepherd R, Denys E, et al. "Onset, natural history and outcome in idiopathic adult motor neuron disease." *J Neurol Sci.* 118:48-55, 1993.

Ratcliff A, Beukelman D. "Preprofessional preparation in augmentative and alternative communication: State of the art report." *Aug Alt Com.* 11,61-73, 1995.

Robbins RA, Simmons Z, Bremer BA, et al. "Quality of life in ALS is maintained as physical function declines." *Neurology*, 56:442-222, 2001.

Saunders C, Walsh T, Smith M. "Hospice care in the motor neuron diseases." In *Hospice: The Living Idea.* Saunders C, Teller J, (eds.) London, England: Edward Arnold Publishers, 1981.

Silverstein MD, Stocking CB, Antel JP, et al. "Amyotrophic lateral sclerosis and life-sustaining therapy: Patients' desires for information, participation in decision-making, and life-sustaining therapy." *Mayo Clin Proc.*, 66:906-913, 1991.

Simmons Z, Bremer BA, Robbins RA, et al. "Quality of life in ALS depends on factors other than strength and physical function." *Neurology*, 55:388-392,2000.

Strong MJ, Grace GM, Orange JB, et al. "A prospective study of cognitive impairment in ALS." *Neurology*, 53:1665-1670, 1999.

Yorkston K, Strand E, Miller R, Hillel A, Smith K. "Speech deterioration in amyotrophic lateral sclerosis: Implications for the timing of intervention." *J Med Speech Lang Pathol.*, 1(1): 35-46, 1993.

Zeitlin DJ, Abrams GM, Shah BK. "Use of augmentative/alternative communication in patients with amyotrophic lateral sclerosis." *J Neuro Rehab.* 9:217-220, 1995.

BIBLIOGRAPHY AND ADDITIONAL RESOURCES

Birbaumer N, Ghanayim N, Hinterberger T, et al. "A spelling device for the paralysed." *Nature* 398(6725): 297-298, 1999.

Mancinelli, JM. "Dysphagia and Dysarthia: The role of the speech-language pathologist." In *Amyotrophic Lateral Sclerosis: A Comprehensive Guide to Management* Mitsumoto H, Norris F (eds.). New York, New York: Demos, 1994.

WORKGROUP PRODUCTS AND TOOLS

Table 1: List of Devices, Manufacturers, and Languages for Communication Assistance

Synthesizer	Languages	Communication device/software
Eurovocs	French, Dutch, German, English, Spanish, Italian	• Eurovocs Suite (Technologie, Ingratie, Inc.) • Dubby (Tash, Inc.) • Speaking Dynamically Pro (Mayer-Johnson, Inc.) • LightWriter (Toby Churchill, Ltd.)
LC Technologies	English, French, German, Norwegian, Swedish	• Eye Gaze (LC technologies)
Gus!	English, Spanish, French, German	• Gus Multimedia Speech System (Gus! Inc.)
KeyWi	American English, British English, Spanish (Latin and Castillian), German	• KeyWi
Infovox	American English, British English, Spanish, German, French, Italian, Swedish, Icelandic, Norwegian, Danish, Finnish	• Speaking Dynamically Pro (Mayer-Johnson, Inc.) • LightWriter (Toby Churchill, Ltd.)
Juno (Apollo II)	English, Irish, French, Welsh, Dutch, German, Italian, Spanish (Castilian and Latin) Catalan, Portuguese, Danish, Swedish, Norwegian, Finnish, Icelandic	• LightWriter (Toby Churchill, Ltd.)

Table 2: <u>Devices that are capable of handling a large amount of digitized speech</u>

<u>Device</u>	<u>Manufacturer</u>
Macaw	Zygo Industries, Inc.
Chatbox	Saltillo Corp
Multi-level Message Mate	Words+
Tech Talk/Tech Speak	AMDI, Inc.
Alpha Talker	Prentke Romich Co.
Black Hawk	Adamlab

Table 3: Internet Resources

- The ALSA Association (www.alsa.org) has links to augmentative communication companies.

- ASHA. The American Speech and Hearing Association (www.asha.org), the professional association of speech and language pathologists in the U.S.
- World Federation of Neurology ALS site (www.wfnals.org) has links to other augmentative communication sites.

- Muscular Dystrophy Association (www.mdausa.org) a number of useful links but specifically:

  - "Used, but not used up: When shopping for durable equipment, second hand isn't always second best." (www.mdausa.org//publications/Quest/q63secondhand.html)
  - "Sorting out speech services" (www.mdausa.org//publications/
- Communication Independence for the Neurologically Impaired (www.cini.org) has information on augmentative and assistive communication and related links.
- ISAAC. The International Society for Augmentative and Alternative Communication, (www.isaac-online.org).
- Rehabilitation Engineering Research Center (RERC) on Communication Enhancement (www.aac-rerc.com).
       This site contains information regarding a number of research projects currently in progress that are supported by a grant from the National Institute on Disability and Rehabilitation Research. It includes comprehensive information regarding Medicare policy for funding ACDs and suggestions to assist speech-language pathologists (SLPs) in writing appropriate documentation. This site has a number of useful links including:
    - Augmentative Communication News. The most widely distributed newsletter in the AAC field. (www.augcominc.com/acn.html)
    - Alternatively speaking. A newsletter for AAC users. (www.augcominc.com/as.html)
    - Augmented Communicators On-Line User Group (ACOLUG). A listserv chat room for anyone interested in AAC.

A number of private individuals have Web sites that provide information for people with ALS that they have found useful. One such Web site is:
- The ALS Survival Guide (www.lougehrigsdisease.net/).

Table 4: Hi-Tech Augmentative Communication Devices Frequently Used by Patients With ALS

Device	Manufacturer
ChatPC	Saltillo Corp.
DynaVox/DynaMyte	DynaVox Systems, Inc.
E Z Keys	Words+
Gus! Multimedia Speech System	Gus, Inc.
Light Writer	Toby Churchill Ltd, via Zygo Industries, Inc.
Link	Assistive Technology, Inc.
Quick Glance	Eye Tech Digital Systems
Vanguard/Vantage	Prentke Romich Co.
VisionKey	H.K. EyeCan, Ltd.

Depression and Pseudobulbar Effects

INTRODUCTION

Patients with ALS will experience symptoms associated with motor neuron degeneration, and therefore, health care providers have several opportunities to begin to prepare the patient for these conditions. Preparing the patient for possible symptoms will help increase the likelihood of initiating symptomatic therapy. Additionally, many patients experience secondary psychological changes that are often not discussed during routine clinical visits. Development of psychological changes may include depression, anxiety and restlessness. Even the impact of coping with pseudobulbar affect, recognized as spontaneous crying or laughing, can have a profound psychological impact on patients with ALS. Onset of psychological symptoms is difficult to prepare for, and these are often upsetting to the family.

WORKGROUP FINDINGS

Identifying the Existing Resources

Depression and Pseudobulbar Affect
Many patients with ALS develop psychological changes, the most common being depression. The frequency of depression in patients with ALS ranges between 11% (Ganzini et al., 1999) to 22% (Houpt et al., 1977). The incidence of depression in ALS may differ between men and women. Specifically, a recent study of the ALS CARE database reported that out of 2,576 patients, as many as 50% of women reported depression as compared to only 36% of men (de Sepulveda L, et al., 2001). This same study also reported that among those with ALS, 24% experienced anxiety. Interestingly, 18% of those who reported anxiety did not have clinical depression. It should be noted that a literature review of MEDLINE, EMBASE and PsychInfo did not reveal any information specific to anxiety and ALS, anxiety if mentioned at all, was combined with depression, insomnia or agitation.

During the course of illness, many patients also develop psychological changes that are clearly due to the disease process, such as the frontal neuronal degeneration that leads to pseudobulbar affect. This manifests in patients as behavioral changes characterized by the symptoms of spontaneous crying or laughing. The lowest incidence of pseudobulbar affect was reported as 2% (6/318) patients with ALS at disease onset (Gubbay et al., 1985). Another study showed that 14/43 patients reported outbreaks of crying and 4/43 patients reported outbreaks of laughter (Newson-Davis, et al., 1999). In the study reported previously, out of 2576 patients with ALS enrolled in the ALS Care database, 15% demonstrated pseudobulbar affect (de Sepulveda, et al., 2001).

Diagnosis and Screening
One reason for differing epidemiological reporting of pseudobulbar affect in patients with ALS is the time at which they are evaluated for the disorder. As the disease progresses, with continued loss of cortical neurons or connections, the likelihood of spontaneous or inappropriate laughing or crying increases—making pseudobulbar affect changes more common with advanced disease. Conflicting reports also arise based on differing nomenclature and definitions. In addition to referring these psychological changes as "pseudobulbar affect," other terms that have been used include "emotional lability," "compulsive crying," or pathologic crying or laughter (Moore et al., 1997; Poeck K, 1969). Consequently, some studies may exclude or de-emphasize inappropriate laughter; this may be reflective of the observation that excessive crying may be more disconcerting to family members or caregivers.

The variance in the epidemiological data regarding psychological changes (i.e., depression and pseudobulbar affect) also may stem from differing methodologies for identifying these changes in subpopulations of patients. Specifically, the report by de Sepulveda and colleagues (2001) used patient

report forms that were independent of health care worker supervision or guidance. In contrast, Clarke and colleagues (2001) used the Hospital Anxiety and Depression Scale to assess the frequency of depression in a small population of patients with ALS. This study reported that the frequency of depression among patients with ALS was within the normal range, but the results were based on a very small group of patients.

Incidence of Depression with Progression of Illness Severity
Clinically, one might assume that as disease progresses with ALS and as patients approach the end of life, the incidence of depression and other psychiatric comorbidities might, theoretically, increase. Consequently, it makes sense to explore the hypothesis that the epidemiology of depression and other psychiatric conditions during the end of life may change as the illness progresses.

Rabkin and colleagues (2000) performed a study in 56 patients with ALS and 31 caregivers. Patients and caregivers were screened for depression, anxiety, distress, and resilience. The results from this small survey showed that neither patients nor caregivers displayed significant psychopathology with respect to depression or depressive symptoms. Depressive symptoms or psychological distress were not time dependent in relation to diagnosis, the amount of disability, or the amount of disease progression. Distress was associated with an interest to hasten death, but willingness to consider assisted suicide was not associated with distress. Interestingly, concordance between the patient and caregiver distress was high, and this suggests that attention should be paid to the mental health of caregivers, which might in turn alleviate the patients' distress. Although this is only a single study done in a small group of patient and caregivers, it suggests that clinical depression or significant depressive symptoms are not inevitable with advanced disease.

Available Tools for Measuring Depression
There are multiple validated scales that will help diagnose depression including the Hamilton Depression Scale and the Beck Depression Index; but there is no single recommended instrument or depression screening procedure specifically for patients with ALS. There are two currently available validated tools for assessing pseudobulbar affect in patients with ALS:
- CNS LS (Moore et al., 1997); and
- Emotional Lability Questionnaire (Clarke et al., 2001; Newson-Davis et al., 1999).

These instruments are not widely used in clinical practice for patients with ALS, and few health care providers are familiar with their implementation and value.

Pharmacological Management
Although limited studies have been done to manage depression, anxiety and other psychological changes during the end of life, appropriate management of these symptoms may be instrumental in achieving a good quality of life for these patients. Ganzini et al. (1995) reported that hopelessness, a common symptom of depression, correlated highly with poor quality of life. Several small studies suggest that pharmacological management may prove helpful in these patients, yet specific studies of management at the end of life are still needed.

Treatment of Pseudobulbar Affect
Iannoccone and colleagues (1996) reported the results from four patients with ALS that received fluvoxamine for treatment of pseudobulbar affect. In this study (which also included MS and stroke), the frequency of outbreaks averaged 30 per day prior to treatment, and was reduced to less than 5 per day with treatment.

Van Driel and colleagues (1998) did a meta-analysis of the treatment of patients with stroke, MS or ALS who were treated with tricyclic antidepressant or selective serotonin reuptake inhibitors. Both treatments

were effective in improving pseudobulbar affect in patients with stroke and ALS; the effect was noted within 7 days of starting treatment.

Treatment of Depression
Bradley and colleagues (2001) reported that in patients registered in the ALS CARE database, only 41% of those who reported depression actually received antidepressants (Bradley et al., 2001). This study was particularly interesting as it included data from several ALS centers, suggesting that successful diagnosis and treatment of depression in this population of patients may be challenging.

Nonpharmacologial Management
The standard approach for nonpharmacologial management of depression and other psychological conditions includes psychiatric or psychological counseling. Many patients ask for and receive education about the disease, including what to expect and how to manage the many aspects of the debilitating illness (see section on Psychosocial Management). However, psychological counseling is only sought by a minority of patients. Specifically, Shiffer and Babigian (1984) reported that approximately 23% of patients with ALS sought psychiatric contact.

Defining The Existing Gaps
- No standardized algorithms are available that instruct how and when health care providers should screen for psychological comorbidities at the end of life in ALS.
- With progression of the disease, testing for depression is clinically more challenging to implement, and tools adapted for end-of-life screening for depression are lacking.
- The clinical benefits of treating depression and pseudobulbar affect are not clear, and not well studied in ALS as related to improving quality of life and improving quality of death for patients.
- Psychostimulants (methylphenidate) for depression at the end stages of other diseases (cancer, HIV) offer therapeutic benefits. However, possible benefits of psychostimulants in ALS at the end of life have not been studied.
- There are no well-defined steps (or protocols) for preparing the patient and families for possible psychological changes that might occur with disease progression in ALS.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
1. Physicians and health care providers should routinely screen for signs and symptoms of depression in their patients with ALS; routine screening for signs of depression are warranted at the end of life.
   - *Early* signs and symptoms of depression may include a sense of hopelessness, lack of interest in previously enjoyed activities, lack of social interactions, changes in sleep patterns, changes in mood, loss of appetite, and loss of libido, among others.
   - As ALS patients approach the end of life, they may be more likely to ask questions on assisted suicide or additional prescription medications.
   - This should be done including psychiatric and psychological consultation with an emphasis on identifying specific clinical characteristics of depression that may help in directing therapy choices.

2. Treatment of depression is an accepted standard of care for other disease states and includes use of SSRIs and tricyclic antidepressants. For some patients with ALS diagnosed with clinical depression, a trial of standard antidepressants (SSRIs or tricyclic antidepressants) may be a treatment option. Although randomized, controlled studies are lacking, previous reports indicate that SSRIs (fluvoxamine) or tricyclic antidepressants may be tried for treatment of pseudobulbar affect (Miller et al., 1999).

3. Counseling also is critical part of care of the ALS patients and their caregivers. In addition to psychiatrists, psychologists and other therapists, experienced nurses and social workers are often very helpful in identifying hidden or subtle signs of depression or even causes of "secondary" depression. Before the health care team engages in a rigorous pharmacological treatment approach using antidepressants or other medications (that can be associated with side effects), patients should be provided counseling opportunities specifically addressing some of the concerns surrounding end-of-life issues for patients and caregivers.

Research Recommendations
1. Develop studies to better understand the epidemiology of depression associated with ALS and the frequency and impact of its comorbidity during the end of life. Additional studies that investigate the cause of depression also are needed. Specifically, it is unclear if depression is endogenous to the disease or is secondary to other factors associated with the illness.
2. Develop a standardized process for diagnosing depression and pseudobulbar affect in patients with ALS.
3. Develop studies to further investigate effective therapies and treatment protocols (including psychostimulants, among others) for treatment of depression and pseudobulbar affect during the end of life in patients with ALS.
4. Drug therapies are specifically needed that will help treat depression and other psychological comorbidities of ALS, including pseudobulbar affect.
5. Routine and standardized screening procedures for changes in mood and affect should be a part of every formal clinic interaction between the health care professionals and their ALS patients, particularly toward the end of life.

Policy Recommendations
1. Health insurance coverage needs to include psychiatric and psychological evaluations of ALS patients at the end of life as well as for their caregivers.
2. Practice parameters and other treatment guidelines for ALS need to incorporate diagnosis and management of psychological distress in patients and caregivers.

REFERENCES

Bradley WG, Anderson F, Bromberg M, et al. "Current management of ALS: comparison of the ALS CARE Database and the AAN Practice Parameter." *Neurology* 57:500-504, 2001.

Clarke S, Hickey A, O'Boyle C, Hardiman O. "Assessing individual quality of life in amyotrophic lateral sclerosis." *Qual Life Res* 10(2):149-158, 2001.

De Sepulveda LB, Sufit R, and the ALS CARE Study Group. "Identification of psychological well-being and depression in an ALS population and those factors influencing its presentation." *Amyotroph Lateral Scler Other Motor Neuron Disord* 2:48-49, 2001.

Ganzini L, Johnston WH, Hoffman WF. "Correlates of suffering in amyotrophic lateral sclerosis." *Neurology* 52:1434-1440, 1999.

Gubbay SS, Kahana E, Zilber N, Cooper G, Pintov S, Leibowitz Y. "Amyotrophic lateral sclerosis. A study of its presentation and prognosis." *J Neurol* 232:295-300, 1985.

Houpt JL, Gould BS, Norris FH Jr. "Psychological characteristics of patients with amyotrophic lateral sclerosis (ALS)." *Psychosom Med* 39:299-303, 1977.

Iannaccone S, Erini-Strambi L. "Pharmacological treatment of emotional lability." *Clin Neuropharmacol.*, 19:532-535, 1996.

Miller RG, Rosenberg JA, Gelinas DF, et al., and the ALS Practice Parameters Task Force. "Practice parameter: The care of the patient with amyotrophic lateral sclerosis (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology." *Neurology* , 52:1311-1323, 1999.

Moore SR, Gresham LS, Bromberg MB, Kasarskis EJ, Smith RA. "A self report measure of affective lability." *J Neurol, Neurosurg, Psychiatr* 63:89-93, 1997.

Newsom-Davis IC, Abrahams S, Goldstein LH, Leigh PN. "The emotional lability questionnaire: a new measure of emotional lability in amyotrophic lateral sclerosis." *J Neurol Sci* 169:22-55, 1999.

Poeck K. "Pathological laughing and weeping in patients with progressive bulbar palsy." *Ger Med Monthly* 14(8):394-397.

Rabkin JG, Wagner GJ, Del Bene M. "Resilience and distress among amyotrophic lateral sclerosis patients and caregivers." *Psychosom Med* 62:271-279, 2000.

Schiffer RB, Babigian HM. "Behavioral disorders in multiple sclerosis, temporal lobe epilepsy, and amyotrophic lateral sclerosis. An epidemiologic study." *Arch Neurol.,* 41:1067-1069, 1984.

Pain Management

WORKGROUP FINDINGS

Identification of Existing Resources

In the ALS CARE database, 20.9% of patients noted pain at the time of initial enrollment into the program (Miller et al., 2000). In a study of ALS patients in hospice, 76% of participants reported pain complaints (Saunders et al., 1981). At the time of referral to hospice, 57% of patients had uncontrolled pain yet only 12% were receiving opioids (O'Brien et al., 1992). Despite these reports of high prevalence of pain in patients with ALS, there is very little available in the literature on pain syndromes or pain management specific to ALS.

Actually, reports on pain in ALS are conflicting, as others describe pain as rare or unusual until the late stages of disease (Francis et al., 1999; Jackson, Brayn, 1998). There is only one article published in 1985 that specifically addresses pain in ALS (Newrick, Langton-Hewer, 1985). Additionally, this review identified 4 articles that discuss symptoms at the end of life in patients with ALS, and among these, pain is mentioned (Saunders et al., 1981; O'Brien, Kelly 192; Oliver, 1993; Oliver, 1996). Two case reports were identified detailing pain syndromes in four patients (Drake, 1983; de Carvalo et al., 1999). In these four patients, chronic pain syndromes appeared at different times during the course of their illness.

One specific study reviewed the correlates of suffering and quality of life in patients with ALS (Ganzini et al., 1999). The median pain severity score on a five-point Likert scale was two, however 20% rated their pain severity as greater than four (out of a maximum of five) suggesting that 20% of patients with ALS have considerable pain conditions. Additionally, as expected, increased suffering correlated with increasing pain. This study also attempted to characterize the types of pain seen in this population. The primary sources of pain were aching musculoskeltal pain of varying sites (61%); cramps (55%); and trauma (24%). The authors note that some patients had more than one type of pain but further details were not given.

Although there are several algorithms available for pain management in other medical conditions, such as cancer, there is a clear paucity of literature that specifically addresses the management of pain in patients with ALS (Figure 1). One important study evaluated the use of opioids for patients with ALS in a hospice setting for management of pain, dyspnea and terminal care. The authors conclude that opioids were well tolerated and effective in reducing the patient's distress; and therefore, warrant their use in this population (Oliver, 1988).

One of the concerns of using opioids during the end of life for patients with ALS is their risk of increasing respiratory depression (Francis et al., 1999; Jackson, Bryan, 1998; Newrick, Langton-Hewer 1985; Borasio, Voltz, 1997). This concern is a known contributing factor to uncontrolled pain in many different illnesses and may be more of a concern to physicians caring for ALS patients given the inherent respiratory insufficiency.

Identification of Existing Gaps
- There is an incorrect perception that pain is not a significant problem in ALS.
- Pain is not consistently screened for or identified in patients with ALS.
- Once pain is identified, there is no consistent or standardized tool to measure the severity of pain or the impact of pain on the patient specifically in patients with ALS at the end of life.
- Once pain has been identified in patients with ALS, there is underutilization of the World Health Organization (WHO) pain management guidelines (Figure 1).

- Health care providers may be uncomfortable with the use of opioid medications in this population of patients with ALS as there are no guidelines on pain management specific for this population of patients.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
As noted, the pain symptoms seen in ALS are typically related to cramps and musculoskeletal aching at varying sites. Many of these symptoms may be successfully managed without opioid medications. It is always appropriate to initiate management with medications that are specifically targeted to the type of pain, regardless of the cause. Patients with moderate to severe pain should have access to opioid medications either alone or in combination with targeted treatments.

The value of non-pharmacological interventions cannot be overstressed. Range-of-motion exercises, frequent repositioning, therapeutic mattresses, relaxation and diversion clearly have a therapeutic role in pain management.

The pharmacological management of pain in ALS is similar to other advanced disease, particularly in the last weeks of life, and currently should be based on the 1990 WHO guidelines. Opioid medications need not be withheld based on the concern of respiratory compromise. The consensus-based recommendations that follow will address management recommendations for the specific pain syndromes that have been identified in patients with ALS; and general principles for the use of opioid medications. Difficulties unique to ALS will be discussed separately.

ALS-Specific Pain Management
- Cramps: Various medications have been used for management of muscle cramps both in ALS patients and other disease processes. These include quinine, diazepam, baclofen, tizanidine and gabapentin.
- Spasticity: The medications that are useful for cramps may also be useful in the management of spasticity.
- Musculoskeletal discomfort: These are often well managed with a non steroidal anti-inflammatory drug (NSAID), aspirin or acetaminophen.

Principles for Use of Opioid Medications
- Careful assessment of pain.
  - This should include location, radiation and description (i.e., sharp, burning etc.).
  - The severity should be assessed using any one of a variety of pain scales.
  - The time course (constant versus intermittent) and any precipitating factors should be elicited.
  - If there is more than one site or type of pain, each should be assessed independently and documented separately.
- Choose a medication appropriate to the severity. As shown on Figure 1, moderate or severe pain (>4 on a scale of 0-10) should be managed with a Step-2 or Step-3 medication. Step-3 medications, such as morphine, do not have a dose ceiling and may be increased as needed until adequate pain control is obtained. It is not necessary to start at Step 1 and progress to Step 3. The choice of medication is determined by the severity of the pain. For example, a patient presenting with level 7 pain and taking no current analgesic can be given morphine.
- Certain medications are NOT recommended for chronic pain management. These include:
  - meperidine because it as a toxic metabolite that causes seizure and delirium;
  - agonist/antagonist agents that have a ceiling effect and an increased incidence of psychotomimetic effects;

- o codeine since it is more constipating and also has an increased incidence of psychotomimetic effects.
- Constant pain requires constant medication. This can be accomplished by scheduled dosing of immediate-release products or sustained-release products.
- Dosing should be based on the pharmacology of the medication and the patient report of efficacy and duration of effect. Immediate-release opioid medications alone or in combination have an effective half-life of three to four hours. Therefore, a four-hour dosing schedule is needed. Tramadol may be given every six hours. Methadone, with its individual variability, initially can be dosed on an as needed schedule.
- Patients on sustained-release medications or continuous parenteral infusions also must have immediate-release medications available for breakthrough dosing.
- Use of adjuvant analgesic agents (e.g., NSAIDS, anti-convulsants, and tricyclic anti-depressants) should be tailored to the specific characteristics of the pain. For example, adding an NSAID for musculoskeletal pain, an anti-convulsant or tricyclic for neuropathic pain, or a muscle relaxant/anti-spasmodic agent for cramps.
- Frequent reassessment of the efficacy of the medication chosen, side effects and need for breakthrough dosing is critical because dosing adjustments and new medications are frequently required.
- Titrate up to reach the therapeutic effect or until development of unwanted/not tolerated side effects. This can be done using one opioid +/- adjuvant medication. There is no indication for more than one sustained-release opioid. Immediate-release medications should all be the same opioid, when possible with the exception of fentanyl.
- Anticipate and manage common side effects, particularly nausea, sedation and constipation (Figure 2). Tolerance will develop to most of these. One exception is constipation. Since this can be a problem for ALS patients not on opioid medications, particular attention must be paid to prevention. Any patient started on opioid medications should also be placed on an aggressive bowel regimen usually including a stool softener and a stimulant.

Problems Unique to Patients with ALS
- Assessment: Obtaining the detailed information needed to complete an accurate assessment may be difficult in patients with impaired speech. In the last weeks of life, pain management focuses on severity. It may be appropriate to establish a way of expressing symptom severity prior to the loss of verbal communication. Non-verbal scales exist but still require pointing to the face or drawing a line on a numeric scale.
- Choice of medication: Many ALS patients have impaired swallowing, therefore the choices of medication may be limited. Sustained-release tablets of morphine or oxycodone cannot be crushed and therefore, are not useful for patients with PEG tubes. The sustained release morphine capsule is a polymer that can be opened and the pellets placed in a PEG, but clogging may be a problem. Alternative routes of administration can be used including rectal use of sustained release tablets, transdermal fentanyl, liquid methadone via PEG, or parenteral (SQ or IV). The majority of patients can be managed without parenteral medications.

Research Recommendations
1. Develop studies that further define specific pain syndromes in ALS including the frequency and severity of these different syndromes.
2. Develop studies that further define the natural history of pain in patients with ALS.
3. Develop studies that further define the impact of pain on quality of life and the association of pain with other concerning symptoms such as insomnia and depression.

4. Support development of clinically tested pain protocols specific to patients with ALS. This specifically should include defining the role and safety of opioids in this patient population at the end of life.

REFERENCES

Borasio GD, Voltz R. "Palliative care in amyotrophic lateral sclerosis." *J Neurol*, 224(4):S11-17, 1997.

de Carvalho M, Mogueira A, Pinto A, Miguens J, Sales LML. "Reflex sympathetic dystrophy associated with amyotrophic lateral sclerosis." *J Neurol Sci.*, 169:80-83, 1999.

Drake ME. "Chronic pain syndrome in amyotrophic lateral sclerosis." *Arch Neurol*, 40:453-454, 1983.

Francis K Bach JR, FK, DeLisa JA. "Evaluation and rehabilitation of patients with adult motor neuron disease." *Arch Phys Med Rehabil.*,80 (8):951-963, 1999.

Ganzini L, Johnston WS, Hoffman WF. "Correlates of suffering in amyotrophic lateral sclerosis."*Neurology* ,52:1434-1440, 1999.

Jackson CE, Bryan WW. "Amyotrophic Lateral Sclerosis." *Semin Neurol.* 18 (1):27-39, 1998.

Miller RG, Anderson FA, Bradley WG, et al. "The ALS patient care database: goals, design, and early results. ALS CARE Study Group." *Neurology* ,54(1):1-8, 2000.

Morley JS, Makin MK "The use of methadone in cancer pain poorly responsive to other opioids." *Pain Rev.*, 5: 51-58, 1998.

Newrick PG, Langton-Hewer R. "Pain in motor neuron disease." *J Neurol Neurosurg Psychiatry*, 48:838-840, 1985.

O'Brien T, Kelly M, Saunders C. "Motor Neuron disease: a hospice perspective." *BMJ*, 304:471-473, 1992.

Oliver D. "The quality of care and symptom control – the effects on the terminal phase of ALS / MND." *J Neurol Sci.*, 139 (S) 134-136, 1996.

Oliver D. "Opioid medication in the palliative care of motor neuron disease." *Palliat Med.*, 12:113-115, 1998.

Oliver D. "Ethical issues in palliative care—an overview." *Palliat Med.*, 7(S 2);15-20,1993.

Saunders C, Walsh TD, Smith M. "A review of 100 cases of motor neuron disease in hospice." In *Hospice the Living Idea*, Saunders C, Summers D, Teller N, (eds.) London, England: Edward Arnold, 1981.

World Health Organization. "Cancer Pain Relief." *Report of the WHO expert committee. Technical report series 804.* Geneva: World Health Organization, 1990.

WORKGROUP PRODUCTS

Figure 1: Guidelines for Management of Pain in ALS

(Adapted from the World Health Organization Pain Management Guide)

```
                          ┌──────────────────┐
                          │   Pain Present   │
                          └────────┬─────────┘
                                   ↓
                          ┌──────────────────┐
                          │ Determine probable cause │
                          │    and severity    │
                          └────────┬─────────┘
                                   ↓
                          ┌──────────────────┐
                          │ Begin appropriate │
                          │ nonpharmacolocial management │
                          └────────┬─────────┘
                    ┌──────────────┼──────────────┐
                    ↓              ↓              ↓
              ┌──────────┐  ┌────────────┐  ┌────────────┐
              │  Cramp   │  │Musculoskeletal│ │ Neuropathic │
              │          │  │    pain     │  │    Pain     │
              └────┬─────┘  └─────┬──────┘  └─────┬──────┘
                   ↓              ↓               ↓
         ┌──────────────────┐ ┌────────────┐ ┌────────────┐
         │ Begin relaxant or │ │Begin acetaminophen,│ │Begin tricyclic or│
         │ Antispasmotic such as │ │  NSAIDs, ASA │ │ anticonvulsant │
         │ Diazepam, tizanidine │ └─────┬──────┘ │  medication  │
         │   or baclofen    │        ↓         └─────┬──────┘
         └────────┬─────────┘ ┌────────────┐        │
                  │           │Uncontrolled pain or│ │
                  │           │ pain score >4/10 │  │
                  │           └─────┬──────┘        │
                  └──────┐          │        ┌──────┘
                         ↓          ↓        ↓
                  ┌──────────────────────────────┐
                  │ Begin opiod mediation or add opiod to current │
                  │  regimen. Begin bowel regimen │
                  └──────────────┬───────────────┘
                                 ↓
                          ┌──────────────────┐
                          │ Titrate to pain relief │
                          └──────────────────┘
```

Figure 2: Guideline for Management of Constipation in ALS

```
                        ┌─────────────────┐
                        │   Constipation  │
                        └─────────────────┘
                                 │
                                 ▼
                    ┌───────────────────────┐
                    │  Assess frequency and  │
                    │  consistency of stool  │
                    └───────────────────────┘
              ┌──────────────┼──────────────┐
              ▼              ▼              ▼
     ┌───────────────┐┌───────────────────┐┌───────────────────┐
     │   Hard stool   ││    Hard stool      ││    Normal stool    │
     │ Normal frequency││ Decreased frequency││ Decreased frequency│
     └───────────────┘└───────────────────┘└───────────────────┘
              │              │              │
              ▼              ▼              ▼
     ┌───────────────┐┌───────────────────┐┌───────────────┐
     │  Begin stool   ││ Begin stool softener││     Begin      │
     │    softener    ││    & stimulant     ││   stimulant    │
     └───────────────┘└───────────────────┘└───────────────┘
              │              │              │
              └─────────┐    ▼    ┌─────────┘
                    ┌───────────────────┐
                    │ No bowel movements │
                    └───────────────────┘
                                 │
                                 ▼
                 ┌─────────────────────────────────┐
                 │ Give or increase dose of stimulant│
                 └─────────────────────────────────┘
                                 │
                                 ▼
                    ┌───────────────────┐
                    │ No bowel movements │
                    └───────────────────┘
                                 │
                                 ▼
                    ┌───────────────────┐
                    │  Give suppository  │
                    │     or enema       │
                    └───────────────────┘
```
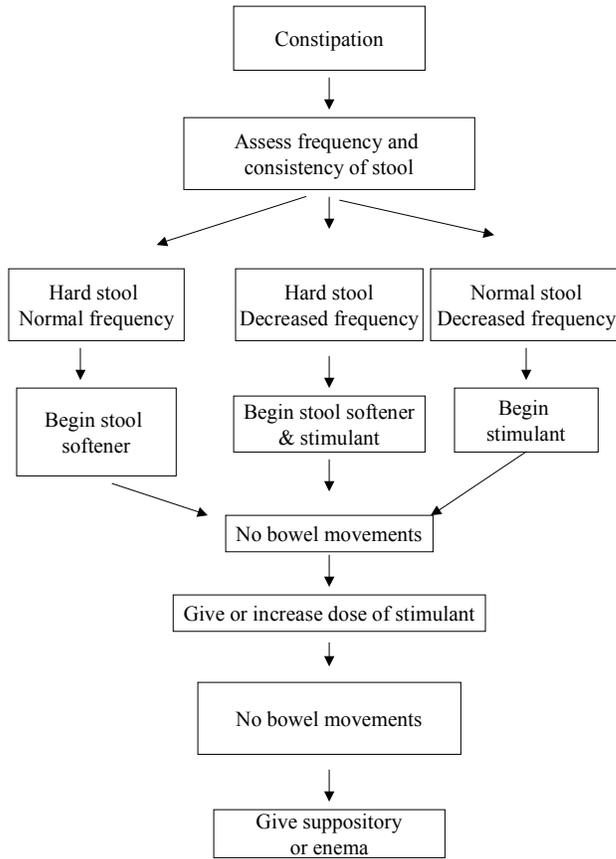
Insomnia in ALS

WORKGROUP FINDINGS

Identification of Existing Resources
Despite the frequency of insomnia in the ALS population, there is very little literature available on the diagnosis and management. There are several articles and abstracts that clearly show the significance of respiratory insufficiency in contributing to insomnia, but the literature also suggest that institution of non invasive positive pressure ventilation (NIPPV) does not resolve the symptom completely (Takekawa et al., 2001; Barthlen, Lange 2000; Pinto et al., 1999; Borasio, Voltz, 1997*)*. For most patients with insomnia, medication is needed but there is no data on the efficacy or safety of specific pharmacological intervention.

Other suggested causes for insomnia are psychic disturbances including anxiety, depression and nightmares; immobility with difficulty changing positions; fasciculation and cramps; and dysphasia with aspiration.

Defining Existing Gaps
- There is inadequate evidence on the diagnosis, incidence, prevalence and management of insomnia in the patient with ALS.
- There is no evidence on the safety and efficacy of medical interventions for insomnia.
- There is no evidence on factors other than respiratory insufficiency that may contribute to insomnia.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
1. One of the major contributing factors to insomnia is respiratory insufficiency. The use of NIPPV can be among the initial management strategies. This is discussed in detail in *Respiratory Care* section of this appendix. Therefore, these recommendations focus on other management strategies either for patients who chose not to utilize NIPPV, do not tolerate NIPPV or whose insomnia is not completely resolved by NIPPV. Non-pharmacological interventions and complimentary and alternative treatments might be useful either alone or in combination with strategies discussed below but no evidence of value exists.
2. The diagnosis of depression should be considered in a sleep disorder. Management of depression-related insomnia focuses on the treatment of the underlying problem, i.e. antidepressant therapy.
   a. Sedating antidepressants may be helpful.
   b. The tricyclic agents (amitriptyline, trazadone, etc.) may be useful for sleep, but the therapeutic doses needed to treat depression are associated with significant potential toxicity.
   c. Of the newer antidepressant agents, mirtazepine (Remeron®) is sedating at low doses and might be particular useful in this setting. There is no specific data available on the use of these agents in the ALS population.

3. In late ALS, nocturnal pain in the hips, shoulders and back is quite common. As patients with ALS weaken, turning and repositioning during sleep becomes more difficult. Typically, although they may fall asleep in a normal amount of time, they awaken after several hours because of hip or shoulder discomfort. Normally, a healthy person arouses and moves in bed without completely waking up. For the ALS patient who has weakened to the point of immobility in bed, they often awaken when they need to reposition. One strategy to help ameliorate the insomnia associated with immobility and discomfort is to use an air mattress, waterbed or a sheet of finger foam to spread the

compressive forces and to try to prevent focal pressure on the hips or shoulders. Sometimes it is necessary for a caregiver to move the patient every several hours.

4.   Pharmacological management to help reduce the pain associated with reduced mobility while sleeping can include the use of an evening dose of medication (NSAID or acetaminophen). The addition of a sedating anti-depressant may also be beneficial. As noted above, amitriptyline, trazadone, or mirtazepine could be useful choices. If these efforts fail, or if the pain is greater than 4/10 on a visual analogue scale (considered "moderate" by the WHO), then a bedtime dose of an opioid can be given. Poorly managed pain is a common cause of interrupted sleep in other populations. Scheduled four-hour dosing or the need for frequent breakthrough dosing may not be a problem during waking hours but may lead to interrupted sleep at night. Use of sustained-release preparations or giving twice the usual dose of scheduled immediate release medications at bedtime can address this concern.

5.   Sleep may also be disrupted by nocturnal leg cramps. Sometimes active or passive stretching of the muscles most likely to be involved is all that is needed. If a medication is required, a nighttime dose of quinine sulfate, baclofen, diazepam or gabapentin is often helpful.

6.   Nocturia may also be problematic, leading to insomnia. Some patients respond to anti-cholinergic agents such as oxybutinin or tolterodine in immediate or sustained-release formulations. As an alternative, during the end-of-life phase, catheterization may be appropriate.

7.   The role of sedative/hypnotic agents in patients with ALS has not been explored. These agents are commonly used for management of insomnia in other populations. Short-acting agents such as zolpidem, or zaleplon, or longer acting agents such as temazepam might be useful in this patient population. Long-term use of these medications is complicated by tolerance, disruption of sleep architecture, and insomnia upon withdrawal.

Research Recommendations
1.   Develop studies that further define the incidence and causes of insomnia in patients with ALS.
2.   Develop studies that explore the relationship of insomnia to quality of life.
3.   Develop evidenced-based algorithms that clearly define effective and safe management of insomnia, particularly in patients who choose not to use NIPPV.

REFERENCES

Barthlen GM, Lange DJ. "Unexpectedly severe sleep and respiratory pathology in patients with Amyotrophic Lateral Sclerosis." *Eur J Neurol*. 7(3): 299-302, 2000.

Borasio GD, Voltz. "Palliative care in Amyotrophic Lateral Sclerosis." *J Neurol* 244(:S11-S17, 1997.

Pinto AC, Evangelista T, de Carhalho M, Paiva T, de Lurdes Sales-Luis M. "Respiratory disorders in ALS: sleep and exercise studies." *J Neurol Sci*. 169(1-2):61-68, 1999.

Takekawa H, Kubo J, Miyamoto T, Miyamoto M, Hirata K. "Amyotrophic Lateral Sclerosis associated with insomnia and the aggravation of sleep-disordered breathing." *Psychiatry Clin Neurosci*. 55(3):263-264, 2001.

BIBLIOGRAPHY

Jacox A, Carr DB, Payne R, et al. *Management of Cancer Pain: Adults Quick Reference Guide. No. 9.* AHCPR Publicaton No. 94-0593. Rockville, MD. Agency for Health Care Policy and Research, US Department of Health and Human Services, 1994.

Care of the Dying Patient with ALS

WORKGROUP FINDINGS

Identification of Existing Resources

The symptoms seen in the last 72 hours of life are similar for many different diseases (Nelson et al., 2000; Adam 1997; Lichter, Hunt, 1990; Brody et al., 1997). In ALS, the majority of patients will have respiratory failure; therefore, this usually is the primary symptom of concern. At the end of life, specifically during the last 72 hours, three symptoms are usually present:
  1) Respiratory symptoms- secretions or dyspnea,
  2) Pain, and
  3) Agitation or restlessness.

The death of an ALS patient usually centers on the respiratory issues. Some patients are on ventilatory support (24-hour non-invasive positive pressure ventilation–NIPPV–or tracheostomy), which will need to be withdrawn. Others will be on no ventilatory support or use intermittent NIPPV. Only recently have a few studies been published that specifically address how to manage respiratory conditions during the last few hours of the patient's life (Borasio, Voltz, 1998; Miller et al., 1999; Neudert et al., 2001; Gelinas 2001).

Identification of Existing Gaps
  • There is ongoing confusion about the legal and ethical issues surrounding the discontinuation of ventilatory support in patients with ALS.
  • Many clinicians and health care providers are neither experienced nor comfortable with the clinical management of patients with ALS during the last days of life.

RECOMMENDATIONS TO THE FIELD

Practice Recommendations
1. As recommended in the ALS Practice Parameters (Miller et al., 1999), there should be a series of detailed discussions with patients and families that includes when decisions should be made for ventilatory support and what to expect. During this time, Advanced Directives should be reviewed. This discussion should be revisited again prior to discontinuing respiratory support. Important points to review and discuss might include:
    a. Descriptions regarding the expected manner and time course of death,
    b. Review of medications that will be used to manage symptoms,
    c. Possible use of sedation, and
    d. Time course of death.
    Importantly, withdrawal of respiratory devices should only occur after discussing this process with the family and other caregivers.
2. Many physicians are not comfortable managing patients through the end of life including discontinuation of respiratory support. Patients on mechanical ventilation are usually not under hospice care and the primary care physician may have little experience with ventilator withdrawal. As a result of this ethical dilemma, patients and physicians would be wise to have discussions regarding the end-of-life process prior to initiating ventilatory support. During the end of life and withdrawal of ventilatory support, the presence of a physician who has an ongoing relationship with the family is very important.
3. Withdrawal of ventilatory support:
    A. General Consideration for withdrawing ventilator: There are several important considerations that will help improve the end-of-life experience for the patient and the family or caregivers:

1. Once the decision has been made to discontinue ventilatory support, and the family/patient have been fully educated on what to expect, every effort must be made to insure that the patients' comfort is maintained.
2. A physician should be present at the bedside for termination of ventilatory support.
3. Discontinuing respiratory support is most often a planned event and therefore, there is no need for haste.
4. All arrangements should be in place prior to the removal of support. Any family members wishing to be present should be nearby.
5. The desire for any cultural or religious rituals should be discussed, planned and implemented.
6. The location should be prepared, if possible, with peaceful lighting and music if desired.
7. If in a home or nursing home setting, all potentially useful medications and suction should be readily available.
8. Parenteral administration of the necessary medications is preferred for rapid onset of action. Unless there is already an indwelling IV in place, the subcutaneous route is preferred.

B. Medical Management of Ventilatory Support Withdrawal (see also Rubenfeld, 2000): Administer opioids for management of dyspnea. Morphine (five to 10 mg if opioid naive) followed by the institution of a continuous infusion. The dose is then titrated to comfort.

1. Administer sedative medications. Benzodiazepines such as midazolam (two to four mg) or lorazepam are commonly used although there are no controlled trials. Chlorpromazine (25 to 50mg) has been successfully used in other populations (McIver et al., 1994). The dose should be titrated to comfort.
2. Anticholinergic medications for secretions should be given if not already in use. Medication choices include glycopyrolate (0.2mg SQ), atropine (0.4mg SQ) or hyoscyamine (0.125mg per PEG).
3. It is ethically appropriate to sedate to unconsciousness but, as noted in the Practice Parameters, muscle-paralyzing agents should not be used (Miller et al., 1999).
4. If oxygen is not already in use, it should not be instituted at this time. If oxygen is being used, FIO^2 should not be increased and discontinuation should be considered. Oxygen can be used for treatment of dyspnea, for comfort, as needed.
5. The physician or nurse should be at the bedside to administer additional medications for comfort as needed.
6. Once comfort has been obtained, end positive expiratory pressure is discontinued, followed by conversion to a T-piece.

C. Medical Management of Patients Not on Ventilatory Support:
The same principles apply as above except medications are initiated in a more gradual fashion since there is no specific event to anticipate.
1) The physician and appropriate other medical hospice health care providers should be readily accessible for medication adjustments.
2) Patients on intermittent NIPPV discontinue use of NIPPV completely.
3) The medication choices are the same as those stated above but can be initiated on an as needed basis as symptoms arise.
4) Medications may be given around-the-clock if distress recurs frequently. All unnecessary medications should be stopped.
5) All monitoring (vital signs, oximetry) should be discontinued. If hospitalized, no further laboratory or X-rays should be done.
6) Oxygen may be used for treatment of dyspnea only for comfort purposes.

RESEARCH RECOMMENDATIONS
1.   To date, there is little data that report how patients with ALS die. This includes information on the prevalence of pain, respiratory failure, anxiety, etc. Prospective studies are needed that provide descriptive data on the end of life for patients with ALS.
2.   Little information is available regarding effective and optimal pharmacotherapies for managing end-of-life symptoms during the last 72 hours. This includes use of analgesics, narcotics, respiratory support, other medications and nonpharmacologic interventions (counseling, spirituality, etc).
3.   Additional educational materials are needed regarding curriculum development for educating physicians about the end-of-life process. This includes an understanding of the symptoms that may be present in the patients such as distress, facial expressions, grimacing, restless movements, visible agitation, etc. Studies need to be done on how to optimally educate the physician who will then need to prepare the caregiver for the end of life of the ALS patient. In turn, the caregiver also may be an important resource in identifying signs of discomfort or distress. This physician, patient and caregiver interaction is unexplored regarding optimizing care at the end of life specifically for the patient.

REFERENCES

Adam J. "ABC of palliative care. The last 48 hours." *BMJ*, 315:1600-1603, 1997.

Borasio GD, Voltz R. "Discontinuation of mechanical ventilation in patients with amyotrophic lateral sclerosis." *J Neurol.*, 245: 717-722, 1998.

Brody H, Campbell ML, Faber-Langendoen K, Ogle KS. "Withdrawing intensive life-sustaining treatment- recommendations for compassionate clinical management." *N Engl J Med.*, 336(9):652-657, 1997.

Cowan JD, Walsh D. "Terminal sedation in palliative medicine-definition and review of the literature."*Support Care Cancer*, 9(6): 403-407, 2001.

Gelanis DF. "Respiratory failure or impairment in amyotrophic lateral sclerosis. Current Treatment Options." *Neurol.*, 3(2):133-138, 2001.

Lichter I, Hunt E. "The last 48 hours of life." *J Palliat Care*, 6:7-15, 1990.

McIver B, Walsh D, Nelson K. "The use of chlorpromazine for symptom control in dying cancer patients." *J Pain Symptom Manage.*, 9; 341-345, 1994.

Miller RG, Rosenberg JA, Gelinas DF, et al. and the ALS Practice Parameters Task Force. "Practice parameter: The care of the patient with amyotrophic lateral sclerosis (an evidence-based review)." *Neurology* , 52:1311-1323, 1999.

Nelson KA, Walsh D, Behrens C, Zhukovsky DS, Lipnickey, V, Brady D. "The Dying Cancer Patient." *Sem Oncol.*, 27(1):84-89, 2000.

Neudert C. Oliver D, Wasner M, Borasio GD. "The course of the terminal phase in patients with amyotrophic lateral sclerosis." *J Neurol.*, 248(7):612-616, 2001.

Rubenfeld GD. "Withdrawal of life-sustaining treatment in the intensive care unit." *Resp Care*, 45:1399-1407, 2000.