

Palliative Care for Patients With Amyotrophic Lateral Sclerosis

"Prepare for the Worst and Hope for the Best"

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THE PATIENT'S STORY

Dr SP is a 56-year-old neurologist specializing in the care of patients with amyotrophic lateral sclerosis (ALS). His past medical and family history are unremarkable. He is married and has 2 adult children. In July 2003, he noticed a right foot drop and experienced mild difficulty walking. In September, he developed some urinary and fecal urgency and weakness in his other foot. Extensive laboratory investigations were unremarkable except for a disk herniation at the thoracic level 6 to 7 with indentation of the cord. The patient underwent a decompression of his thoracic spine in September 2003 and subsequently had 2 additional surgeries for persistent herniated disk at the same thoracic level. In mid-May 2004, his right arm became weak. An electromyographic study showed denervation in the right leg muscles and chronic reinnervation changes in multiple myotomes in the right upper and lower extremity. Neurological examination showed muscle atrophy in both legs and increased muscle tone in all extremities with generalized pathological hyperreflexia. He walked with spastic gait. Sensory examination was completely normal. His forced vital capacity was 4.97 L or 109% predicted with a maximum inspiratory pressure (MIP) of 60 mm H₂O or more. He was given a diagnosis of ALS and self-referred to an ALS multidisciplinary clinic at a university medical center for further management.

He was treated with riluzole, celecoxib (then in use in a clinical trial), and several medications for urinary urgency and spasticity. Extensive recommendations were made by the ALS treatment team to maintain his function at home and at work, including proactive suggestions for respiratory, nutritional, and communication issues.

See also Patient Page.

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Amyotrophic lateral sclerosis (ALS) is a devastating terminal neurodegenerative disease with a highly predictable clinical course such that palliative care should begin at or soon after diagnosis. The outcome is certain in most cases. The only medication approved for treatment in the United States, riluzole, extends life by about 2 months. Virtually all skeletal muscles eventually are affected. Multiple problems require a multidisciplinary approach including aggressive symptomatic management, rehabilitation to maintain motor function, nutritional and respiratory support, augmentative communication devices, and psychological support for both patients and families because family members so often play a central role in management and care. Social, bioethical, and financial issues as well as advance directives should be addressed long before enteral feeding or assistive ventilatory support might be considered. Goals of care should be assessed on an ongoing basis. Presenting the unusual case of a patient with ALS who is also a prominent neurologist specializing in ALS, we enumerate issues in management and palliative care applicable to ALS but also to other fatal, progressive neurologic diseases such as Huntington's chorea and late-stage Parkinson disease.

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By July 2004, his speech became difficult. His course was complicated by deep venous thrombosis, and he started taking oral warfarin. By January 2006, he could no longer talk; he began to use an alphabet board with a laser pointer attached to his eyeglasses to communicate. He used glycopyrrolate to help dry saliva but developed constipation. He lives at home with his family and hired help in the home. Night-time oxygen desaturation prompted initiation of a noninvasive ventilator. Additional medications included omeprazole, lactulose, loratadine, bupropion, and budesonide nasal spray. He also took 1200 mg of Coenzyme Q10 four times a day, vitamin E and α -lipoic acid. His condition has continued to deteriorate with more generalized muscle weakness and spasticity. In January 2006 his forced vital capacity was 1.88 L or 42% predicted with a maximum inspiratory pressure of 60 mm or higher. By the spring of 2007 he had become completely paralyzed but has been relatively stable in the past year. He can still use his eyes to communicate using an alphabet board and has done so recently in a public speech.

Dr SP was interviewed by a Perspectives editor on March 29, 2006, with his wife and son by his side. Using a laser pointer attached to his eyeglasses, Dr SP pointed to letters on an alphanumeric board, spelling out the words of his answers, which were repeated aloud by his son and wife for confirmation. After an initial few minutes of orientation, this seemingly laborious mode of communication smoothed to near conversational speed, as is apparent from the sophistication and complexity of the responses.

PERSPECTIVES

DR SP (THE PATIENT): *Each day focus on what you can do . . . I've always tried to prepare for the worst and hope for the best. . . . Neurologists don't like surprises. They like everything planned out very carefully . . .*

TP (THE PATIENT'S WIFE): *We've pretty much put our lives on hold and SP is our primary focus. . . . We try to enjoy something every day, even if it's just a TV show or a movie, a trip to the sunshine or the beach . . .*

DR A (THE TREATING NEUROLOGIST): *We don't want to do anything to increase the quantity of someone's life if the quality cannot also be increased . . .*

The diagnosis of ALS carries with it an inevitably fatal prognosis. In the absence of curative treatments, the focus is on enabling the patient to achieve maximal function and independence at each stage of illness by providing relief of the multiple symptoms that develop over time.¹ Patients diagnosed with ALS thus require palliative care, which, broadly defined, "seeks to prevent, relieve, reduce or soothe the symptoms of disease or disorder without effecting a cure."² Because no single specialist can address the myriad problems that develop as the illness progresses, multidisciplinary teams are essential in providing optimal comprehensive care. Clinicians face a delicate balance in effectively managing the multiplicity of symptoms, while preserving the dignity and autonomy of the patient and minimizing the fears of the pa-

tient and family. Invasive technologies may prolong life for patients at the very end stages of ALS if the patient so chooses, although most do not. Research participation can provide patients a sense of hope that they can make a vital contribution to understanding the etiology and treatment of ALS.

Presenting the unusual case of an ALS patient who is also a prominent neurologist specializing in ALS, we enumerate issues in the management and palliative care applicable to ALS but also to other fatal, progressive neurologic diseases such as Huntington's chorea, progressive supranuclear palsy, and late-stage Parkinson disease.

ALS: Diagnosis, Prognosis, Etiology

Amyotrophic lateral sclerosis is a progressive neurodegenerative disorder of unknown cause and pathogenesis, with no known cure.³ It is characterized by progressive loss of motor neurons; up to 80% may be lost before the first clinical symptoms appear.⁴ Incidence is 0.2 to 2.4 cases per 100 000 population, with men more often affected than women and whites more than nonwhites.⁵ Onset usually occurs in middle and late life. More than 90% of cases are sporadic while 5% to 10% are familial (predominantly autosomal dominant).³ Among cases of familial ALS, 15% to 20% are attributable to the *SOD1* gene mutation (although other mutations also have been recognized).⁶ While the etiology remains unknown, several plausible hypotheses are currently under investigation.⁷⁻¹¹

Diagnosis in early stages may be difficult and is often made 9 to 11 months¹² or longer¹³ after symptom onset. Diagnostic criteria (El Escorial Diagnostic Criteria-Revised, <http://www.wfnals.org>) require signs in more than 1 of 4 body regions, evidence of both lower and upper motor neuronal degeneration, and progressive spread within or between regions. There is no definitive diagnostic test. Median survival is about 3 years and 5- and 10-year survival is 8% to 16% in the absence of long-term mechanical ventilation (LTMV).¹⁴ With LTMV, survival can be 15 years or longer.¹⁵

Both presenting symptoms and course vary considerably. Limb weakness is the initial symptom for about 60% to 80% of patients,^{16,17} as it was for Dr SP. As noted by Rowland et al,³ painless difficulty with buttons or turning a key are ominous symptoms in midlife. Although there are no typical stages, the weakness becomes more severe and more areas of the body are affected over time, perhaps with muscle cramps and weight loss. The course is progressive with no periods of remission. Stable plateaus are rare.³ Nearly all systems may become involved eventually, except for sphincter control and eye movements which are usually but not always spared. In the United States, most patients do not choose to use LTMV and usually die of respiratory failure.

As in all terminal diseases, predicting how long a patient will live is difficult, although older age at onset and bulbar presentation are negative prognostic factors.^{4,18} In late-stage illness, loss of respiratory capacity is used as a criterion for hospice eligibility, implying a prognosis of 6 months or less.¹⁹ Timing of discussion of advance directives and treat-

ment preferences must be tailored to the individual's illness course, readiness, and imminence of respiratory crisis.

The only US Food and Drug Administration–approved treatment for ALS is riluzole, prescribed 50 mg, orally twice daily, which extends survival by about 2 months.²⁰ Neurologists appreciate the availability of this approved medication for its role in offering patients hope, making the diagnosis more tolerable. Fatigue is a common adverse effect, and modestly elevated liver enzymes also may occur. Other medications are being tested in ongoing clinical trials.

Arriving at the Diagnosis of ALS

DR SP (THE PATIENT): *I knew ALS was the most likely diagnosis by far. . . . I came to accept the diagnosis before sharing with family and friends.*

Exploring Alternatives

In its early stages, making the diagnosis of ALS can be difficult, and false-negative diagnoses by generalists are high.²¹ The neurologist to whom the patient is referred must first determine that all alternative and treatable diseases, such as spondylitic myelopathy, Lyme disease, and multifocal motor neuropathy, have been excluded.²² Ruling out alternative diagnoses may entail surgery, as in the case of Dr SP, or other costly and invasive procedures.^{23,24} However, with an incurable fatal disease like ALS, if alternative plausible diagnostic options exist, we believe such efforts are justified.

Disclosing the Diagnosis

As McCluskey and colleagues²⁵ noted, “imparting the diagnosis of ALS is a formidable task.” In their mail survey of 94 patient-caregiver pairs, 50 patients, and 19 caregivers, only 44% of patients and 52% of caregivers rated the physician's manner of breaking the news as good or excellent. Additional problems reported by participants in the survey related to failure to discuss symptom management, ALS patient assistance organizations, or clinical trials. As with any serious disease, when the diagnosis is delivered, a relative or friend should be present, and the physician should determine what the patient already knows or expects before proceeding. Sensitivity and compassion as well as a positive message are essential.²⁶⁻³⁰ Among those messages are that ALS is not contagious, that there are interventions to manage nearly all symptoms as they evolve, and that a great deal of educational information is available. The patient and family should be assured that much can be done to provide comfort and care, that decisions will be jointly made, and that the physician will always be there for them. Patients and accompanying family members or friends may not remember any details presented at this time, but they never forget the tone and the underlying message of hope and assurance of continued care rather than despair and abandonment.³⁰ BOX 1 provides some suggestions to guide these discussions, which are based on our clinical experience.

The neurologist should schedule a follow-up meeting within a couple of weeks. At that time, discussion should focus on

management of initial symptoms and an overview of problems to anticipate (eg, making safety changes in the house). Specific information, including written materials, referral to support groups and to Web sites is timely (See <http://www.jama.com> for additional resources). Preliminary discussion of advance directives and end-of-life issues may be broached.

In the case of Dr SP, the diagnosis was initially uncertain and a series of surgeries were undertaken. When these procedures had no effect, the patient himself made the diagnosis of ALS and then went to see a neurologist specializing in ALS for evaluation. In fact, he said, “I warned the neurologist that I thought I had ALS. I wanted him to be sure he would be comfortable with me as a patient before I saw him.” After the initial diagnosis was confirmed Dr SP was referred to an ALS multidisciplinary center, where he receives ongoing care.

Role of the Interdisciplinary Clinic and Team

TP (THE PATIENT'S WIFE): *When we go to the ALS Center, he sees the physical therapist and . . . the occupational therapist . . . the nurse and . . . the doctor. They review his medicines and test his strength. They tell him what's on the horizon for ALS research. A social worker will meet with him and/or me. The speech and communication therapist will meet with us. . . . The dietitian meets with us and they weigh him. Also the respiratory therapist measures his breathing. They're very, very thorough.*

Interdisciplinary ALS Clinic

Specialized ALS centers and clinics can provide comprehensive care by addressing diverse issues ranging from purely medical concerns to psychosocial and financial issues and advance planning.^{31,32} There are 76 multidisciplinary ALS clinics throughout North America certified by voluntary disease organizations, such as the ALS Association and Muscular Dystrophy Association (ALS Division). A comparison between multidisciplinary care and standard care in the Netherlands found that patients receiving multidisciplinary care were more likely to receive adequate aids and appliances and scored significantly higher in the domains of social functioning and mental health.³³

A US database of ALS multidisciplinary care was used to compare more than 6000 patients with 111 patients who received care in the community and recorded their experiences via a Web-based registry.³² Those not receiving multidisciplinary care received fewer symptomatic treatments (eg, therapy for drooling received by 3% vs 32% in multidisciplinary clinics; treatment for pseudobulbar affect received 5% vs 24%). Patients cared for in the community reported higher rates of insensitive delivery of diagnosis (46% vs 2%).³² Overall, care in multidisciplinary clinics is associated with enhanced quality of life by alleviating symptoms³⁴ and may extend survival.³⁵

Members of the multidisciplinary team may include a neurologist expert in ALS care, ALS nurse specialist, physical

Box 1. Words to Say Based on the Authors' Clinical Experience**Presenting the Diagnosis: Breaking the News**

"Considering everything, the most likely diagnosis is ALS [amyotrophic lateral sclerosis], although there are no laboratory tests that tell us this definitively."

"ALS is often called Lou Gehrig's disease in the United States, or motor neuron disease and is one of the neurodegenerative diseases, something like Alzheimer disease or Parkinson disease. It attacks healthy adults, causing progressive paralysis of muscles of the body. Despite years of research, we still don't know its cause or have a cure. This doesn't mean we can't do anything. We can do a great deal about the disease at an ALS Center."

"You can call me or any of my staff at any time. We will keep in touch very closely."

Prognosis

"The prognosis varies from one individual to another. Roughly 50% of patients die within 3 to 4 years after the beginning of the symptoms. About 10% to 20% of patients live beyond 10 years, and very few patients live beyond 20 years. A number of factors are associated with slow progression of the disease." (It is helpful to share a couple of factors associated with better prognosis.)

Discussing Percutaneous Enteral Gastrostomy Feeding (PEG)

"Nutritional care is so important. In fact, you may burn more calories than before because you may use more muscles to perform routine activities than before. You may also have muscle cramps, stiffness, and twitching, all of which consume extra energy. Besides moving your body, your muscles store energy the body needs quickly. When muscles become wasted, they can't store as much energy. Weighing yourself weekly will help you monitor your body's caloric needs."

"Obtaining nutrition through a feeding tube reduces eating time, which can take an hour or more. Some patients stop eating because they get so tired. Tube feeding provides all the nourishment you need and can even restore lost weight. This is important because weight loss is associated with decreased respiratory capacity and shorter survival."

"PEG has its risks: infections at the site of the tube, disfigurement of body shape, and diarrhea or constipation that may not always be transient. Tube feeding is cumbersome and with loss of hand movement requires an assistant at every meal. Deciding against tube feeding is okay. You won't starve without it. Your body will adjust and you won't feel hunger; however, many patients have said, 'Wow, why didn't I do this sooner?'"

Recommending Noninvasive Ventilation

"Many assistive devices can greatly help your breathing, which left unassisted may decrease your energy levels and impede your sleep at night. One such device is a noninvasive positive-pressure ventilator. It includes an easy-to-use mask that fits on your face. It should increase energy and provide better sleep."

Discussing Tracheostomy and Long-term Mechanical Ventilation

"Eventually, you may need more assistance with your breathing. You could consider undergoing a tracheostomy and receiving long-term mechanical ventilation (LTMV), a decision that will involve your whole family and that requires thoughtful evaluation."

"With tracheostomy and LTMV breathing becomes easier, aspiration pneumonia becomes less likely, and survival is prolonged, which may be important for those with specific life-time goals."

"As your disease progresses, you may reach a 'locked in state,' making communication impossible. Some patients who can speak before the procedure are not affected, but others can't speak after tracheostomy. Frequent mechanical suctioning is needed to remove secretions. This essential procedure causes transient gag and discomfort. Very few patients have infection or bleeding. For those who use a high-pressure cuff on the airway, tissue damage of the trachea may rarely occur. The costs for home care and equipment not covered by insurance are high. Handling the necessary equipment and performing procedures require a lot from caregivers. The equipment requires permanent placement of a tube, which is continuously connected to a machine, in the upper airway at your neck. Portable machines are available so that patients may go out."

"This is a decision that is best made long before you might suddenly need it so that your family knows your wishes. We can give you a lot of information and lend you a video to give you a better idea of what the experience might be like. If you find that living with an LTMV is not acceptable, you have the legal right to discontinue it. You should have an advance directive informing us of the circumstances under which you don't wish to continue on the machine."

Recommending Hospice Care

"I wish I could use hospice service as early as possible, preferably as soon as the diagnosis of ALS is made, although the hospice rules do not provide for that. Hospice, which is covered by Medicare, provides the best palliative care and comfort. At home services, include visits by a nurse, social worker, or chaplain; some home health aide coverage; and 24-hour on-call nursing. We work with the hospice team because we are responsible not only for maintaining your function, quality of life, and dignity but also for making you comfortable."

therapist (to help manage spasticity), occupational therapist, dietitian, speech pathologist (to explain and order communication devices), pulmonologist or respiratory therapist, social worker, patient service coordinator from voluntary disease organizations, research coordinator, mental health

professional, gastroenterologist, interventional radiologist, orthotist (to evaluate and select or fabricate personalized limb braces) and prostho-odontist (to evaluate and fabricate a palatal lift to improve nasal speech). Often, 5 or 6 different specialists see the patient on the same visit. Dete-

rioration is often faster than the patient and family anticipate, and professionals can help them to identify and adjust to these changes. Staff members can help patients to obtain insurance coverage that is initially denied and to negotiate the best possible care. Psychosocial and spiritual needs, such as anticipatory mourning, may be addressed by the social worker or the team member with whom the patient or caregiver is particularly close. Once hospice is initiated, pastoral counselors are available for home visits.

Progressive Nature of ALS: Symptom Management

DR A (THE TREATING NEUROLOGIST): *Everything we recommend is aimed at trying to do both [address quality as well as quantity of life]. Because he is aware of the importance of nutrition, [Dr SP] has been meticulous about weighing himself and not losing weight. A lot of the credit goes to his family. . . . they spend hours every day feeding him. . . . That's why he has agreed to getting a PEG tube, because that will . . . hopefully free up precious time for him and his family that he won't need to spend eating.*

From the outset, patients should be reassured that many solutions have been devised for the multiple problems that may evolve. Symptoms that may develop in no particular order include limb weakness,¹⁶ cramps,⁴ spasticity,³⁶ pain,³⁷ dysarthria, sialorrhea,³⁸ fatigue and insomnia,³⁹ depression,^{10,40,41} fear and anxiety, involuntary emotional expression disorder,^{39,42} constipation, aspiration,⁴³ and laryngospasm.⁴⁴

Cognitive Impairment. Traditionally ALS was believed to spare memory and cognition,⁴⁵ but as many as half of patients with ALS may have at least mild cognitive impairment.⁴⁶ Disturbances in frontal lobar function have been reported in 28% to 48% of patients with ALS.⁴⁷ Frontotemporal dementia (FTD) has been specifically associated with ALS.⁴⁸ Its diagnosis, using the Neary criteria that include early loss of insight, and supportive diagnostic features such as mental rigidity,⁴⁹ is complicated by the range of disabilities due to ALS (eg, inability to speak or write). Although untreatable, FTD is important to recognize because its presence may substantially interfere with the patient's capacity to make treatment decisions.⁵⁰

Although decisions to initiate supportive interventions to help the patient cope with symptoms of the disease are nearly always straightforward, management of nutritional insufficiency with enteral feeding and of respiratory insufficiency with noninvasive ventilation (NIV) or LTMV are more complicated, more enduring, and can be more controversial. Patients may want to postpone percutaneous endoscopic gastrostomy (PEG) or they may refuse it outright. Although, in our experience, most patients accept NIV, LTMV raises more issues. The rapid progression of ALS can make adjusting to new treatment decisions difficult for patients and families, but delay in advance care planning can make some interventions less effective or no longer possible (eg, PEG placement after respiratory deterioration). The challenge for the physician is to help ensure that the patient receives desired treatment but not exert undue pressure before the patient and family are ready.

Nutritional Care and Enteral Feeding. Good nutrition and hydration are essential for well-being and indeed, survival.⁵¹ Difficulty eating is often associated with weight loss and is a common problem for ALS patients. As swallowing difficulty increases, each meal can take an hour or more and taking oral medication becomes problematic. In our experience, a PEG reduces this burden on both patient and caregiver, so more calories can be consumed with benefit to general health and stamina. The American Academy of Neurology Practice Guideline,⁵² using evidence-based medicine, recommends that PEG be considered for those with dysphagia and weight loss, although many neurologists remain reluctant.^{53,54} Ways to approach discussing PEG placement are provided in Box 1. A PEG can be most safely placed when respiratory capacity is still greater than 50% of predicted.⁵² Although there have been no randomized trials to demonstrate that PEG prolongs survival, malnutrition is an independent risk factor for a worse prognosis in ALS.^{14,55} In a study of 55 patients, low body mass index substantially increased risk of death.⁵¹ Dr SP decided to have a PEG, as reported in his physician's interview.

Dyspnea. Shortness of breath occurs when the muscles of respiration become weak. It may be the presenting symptom or may develop years later, first occurring on exertion and then when lying down. Later it may cause or exacerbate insomnia. When respiratory difficulty begins to interfere with sleep or forced vital capacity declines substantially (usually below 50% of predicted), NIV is usually recommended.⁵² More recently, maximum inspiratory pressure⁵⁶ or nasal sniff pressure⁵⁷ has been found to be more reliable than measuring forced vital capacity. In our experience, nearly all patients agree to try NIV when advised to do so. Sometimes patients with severe bulbar dysfunction cannot tolerate it while others leave installed equipment unused. Longitudinal studies show that NIV can prolong life approximately 12 to 18 months⁵⁸ and improves its quality by alleviating shortness of breath, improving sleep, and increasing mental alertness and energy to pursue social activities.⁵⁹ In a randomized trial, NIV lengthened the time that quality of life scores remained above 75% of baseline by at least 3 months compared with those receiving standard care.⁵⁸ In an observational study, scores on a standardized quality of life measure increased as much as 25% after initiation of NIV for 16 patients, despite disease progression, compared with a control group of 11 patients who declined NIV.⁶⁰ Later in the course of the disease, treatment to extend life requires tracheostomy and LTMV, which sustains respiration indefinitely, although disease progression continues unabated.⁶¹ LTMV is discussed in greater depth below.

Impact of ALS on Informal Caregivers, Family, and Friends

TP (THE PATIENT'S WIFE): *This family of ours pulled together and is really strutting its stuff. These children are wonderful. We're a very close family. SP set us up that way. . . . We've pretty much put our lives on hold and SP is our primary focus.*

Box 2. Approximate Costs of Various Interventions for Patients With Amyotrophic Lateral Sclerosis^a

Costs Related to Percutaneous Enteral Gastrostomy Feeding

Gastroenterologist consultation: \$500
 Procedure: \$2200 to \$2400
 One-day hospital admission: \$3950
 Food (6 cans of 8-ounce Ensure Plus): \$260 per month
 Enteral pump rental: \$560 per month

Respiratory Aids

Noninvasive ventilator: \$6000
 Mechanical volume ventilator: \$18 000
 Pulse oximeter: \$1200
 Apnea monitor: \$4600
 Suction machine: \$375
 In-exsufflator: \$6500

Mobility Aids

Manual wheelchair: \$600
 Low-tech power wheelchair: \$5000 to \$8000
 High-end power wheelchair: \$10 000 to \$40 000
 Hoyer mechanical lift: \$1000

Communication Aids

Augmentative device
 Low-tech: \$200 to \$1500
 High-tech: \$4000 to \$15 000

Medication

Riluzole, 50 mg taken orally twice daily: \$550 per month

Home Assistance

Registered nurse: \$50 to \$75 an hour
 Licensed practical nurse: \$35 to \$45 an hour
 Home health aide: \$15 to \$20 an hour

^aThese costs are based on 2007 information from vendors in the New York City area. Cost varies by location, as does insurance coverage for the listed items.

WP (THE PATIENT'S SON): *I'm thankful my family was financially secure enough that I could move home and not have to work another job to help support my family. I can spend my time not only helping him but also spend time just being with him.*

Caregiving Responsibilities. Although caregivers of all seriously ill patients with medical conditions or dementia face complex demands,⁶² perhaps no caregivers are more challenged than those of ALS patients. With progressive disease, patients with ALS need increasing levels of assistance with nearly all activities of daily living.⁶³ In addition, their ability to communicate diminishes and the physical demands of their

care get more onerous at the same time that it becomes less safe to leave them unattended.⁶⁴ The household requires drastic changes, and, if financially able, family members may have to stop working to provide care. Ironically, the insured family member may be unable to stop working because family health insurance is job related. Despite their own need for support, caregivers may be unable or unwilling to attend support groups or counseling so that they may stay home with the patient. Even with paid assistance, ALS caregivers are estimated to spend an average of 11 hours per day with the patient.⁶⁵

Emotional Burden. In studies involving ALS patients and caregivers, factors independently related to caregiver's perceived burden are the degree of the patient's disability and disease duration (themselves correlated), which is not necessarily alleviated by participation in support groups or number of available substitute caregivers.⁶³ In another study, a global measure of caregiver distress was found to increase over time and to be exacerbated by the patient's emotional lability, number of other dependents, and negative (critical) feedback from social network members.⁶⁶ Caregivers who reported greater burden also reported more depressive symptoms, although frank clinical depression was the exception.^{63,67}

Impact of the Patient on the Caregiver. In contrast to patients with Alzheimer disease, whose caregivers are the most studied, ALS patients retain the capacity to appreciate caregiving, to express affection, and to actively participate in their lives and relationships even if mute or immobile. Thus, caregiver burden can be profoundly offset when satisfaction with caregiving is high, and this is often related to the appreciation the patient provides to the caregiver.^{68,69}

Financial Aspects and Burden of Care. Out-of-pocket costs for families with ALS patients are great. Costs for mechanical ventilation and 24-hour care range up to \$200 000 a year (BOX 2).^{61,70} For those without pharmaceutical coverage, out-of-pocket costs for riluzole are about \$550 per month to achieve an average 2 additional months of life.

The goal of preserving the patient's quality of life and autonomy at home for as long as possible requires expensive equipment and home renovation including power wheelchairs, rotating beds, powered seat lift recliner chairs, a mechanical lift, specialized computer equipment, a vehicle equipped with hand controls, and a van equipped with ramp and lift. Although some items are covered by insurance, out-of-pocket expense can amount to thousands of dollars per year. Box 2 presents costs of equipment and services provided by vendors in the New York City area. The extent of insurance coverage depends on the patient's policy. It is crucial to have an experienced ALS team work with patients and their families to provide advice regarding effective use of their insurance coverage. The Muscular Dystrophy Association and ALS Association can provide limited support.

Professional Staff Support

DR A: *The one thing I want to emphasize is that working with these patients has always been hard . . . in this line of work where*

every person with the disease will die eventually. . . . I also really value the support groups that we have with our staff. . . . I feel like I'm in here for the long haul and I want to pace myself, and I want to pace our team.

Dr A highlights the staff stressors and coping strategies to avoid burnout. It is important to recognize one's own vulnerability to burnout and to recognize signs of stress.⁷¹ Team philosophy, team support, and collective coping strategies are significant factors in maintaining the individual staff member's sense of competence and motivation. Those who specialize in caring for patients with ALS often know their patients for longer than palliative care specialists. Thus, when a patient with ALS dies, the loss experienced by ALS professionals can be even more profound.⁷²

Tracheostomy and LTMV

DR A: *A lot of times patients don't have to make that decision [whether to prolong life by means of LTMV] . . . For most of my patients who have had to make that decision, it has been easier because at that point they are so disabled by their disease that they're just ready to go. It's usually not an agonizing decision.*

In ALS, respiratory capacity eventually fails, even with NIV. Patients and families are faced with deciding about LTMV intervention, and advance planning is essential to preclude unwanted emergency tracheostomy in a crisis. With LTMV, patients eventually may reach a "locked in" state in which they cannot communicate at all.¹⁵ This may be a circumstance in which patients would desire discontinuation of ventilation but unless clearly specified in advance, decisions about how to proceed become highly problematic.

Prevalence of LTMV is influenced by treating physician attitudes, insurance coverage (national or private), and cultural standards (eg, whether the physician, the patient, or the family makes the decision) and so varies substantially both between and within countries.⁷³ In North America, refusing life-sustaining measures (like LTMV in the context of respiratory failure) is both legal and considered respectful of the patient's right to choose according to the ethical principle of autonomy, as is the right to discontinue such life-sustaining measures.

A US study (n=1458) found a rate of LTMV use of 2%,³⁴ while in an English sample (n=50) the rate of LTMV was 0 at a time when national health insurance did not cover home ventilation,⁷⁴ and 3% in a German study of 121 patients.⁷⁴ In contrast, in a 2004 study in Japan, the rate of LTMV was 27%.³¹ The rate in Japan appears to be increasing, perhaps related to financial considerations (the Japanese government covers costs of LTMV), physician support for LTMV, social pressure from the Japanese ALS Association, and differences in cultural attitudes about "truth-telling" and death. Historically, Japanese patients and families expected the doctor to determine treatment strategies and decisions, at least until quite recently.^{31,75}

Rates of LTMV also vary considerably within country. A study conducted in the early 1990s in the United States found that the percentage of ALS patients receiving LTMV at dif-

Box 3. Triggers for Initiating Discussion About End-of-Life Issues in Patients With Amyotrophic Lateral Sclerosis Including Prognosis, Advance Directives, and Hospice^a

The patient or family asks—or opens the door—for end-of-life information and interventions (elicited or spontaneous, verbal or nonverbal)

Severe psychological, social, or spiritual distress or suffering

Pain requiring high dosages of analgesic medications

Dysphagia requiring feeding tube

Dyspnea or symptoms of hypoventilation or a forced vital capacity of 50% predictable or less

Loss of function in 2 body regions (regions include bulbar, arms, and legs)

^aBased on consensus among 20 ALS experts.¹

ferent treatment centers ranged from 1.4% to 14% and was related to physicians' own attitudes toward its use.⁷⁶ However, not all tracheostomies are planned or voluntary. In fact, Moss et al⁷⁷ speculate that only a minority of those receiving LTMV makes this choice in advance, and in their study of 50 patients assisted by LTMV, fewer than half had done so. In a German survey, 66% of patients receiving LTMV had emergency intubation, and 81% did not give informed consent for the procedure.⁷⁸ In a longitudinal study of 80 patients with ALS whose expected survival was less than 6 months and who were patients in our own clinic, 14 of 80 (18%) electively received LTMV, an unusually high rate that may be partly due to their late stage of illness at study entry.⁷⁰ After tracheostomy, 50% identified circumstances in which they would wish to discontinue treatment, such as having to go to a nursing home, being locked in, or becoming demented. In a prospective study, Albert et al⁷⁹ found that patients with ALS had clear preferences for or against tracheostomy and LTMV well in advance of the point of crisis and that these preferences were related to actual outcomes.

Although no research has explored the tradeoffs of choosing or refusing LTMV by ALS patients, preferences regarding acceptance or rejection of treatment by seriously ill older patients have been studied in hypothetical scenarios.⁸⁰ Although 99% would choose a low-burden treatment with return to current health status, most preferred death over survival when their condition after treatment would entail severe functional or cognitive impairment, even when the treatment was not high burden. In another study,⁸¹ community residents who ranged from well to terminally ill were given 5 hypothetical health states and asked about life-sustaining preferences. Across groups, treatment was refused when the hypothetical health outcome was regarded as worse than death. In both studies, defining states worse than death was a subjective judgment determined by per-

Box 4. Medicare Hospice Entry Criteria for Patients With Amyotrophic Lateral Sclerosis**Patients Must Meet at Least 1 of the Following Criteria**

1. Critically impaired breathing capacity as demonstrated by all of the following:

- Forced vital capacity less than 30% of normal
- Dyspnea at rest
- Patient declines mechanical ventilation

2A. Patient should demonstrate both rapid progression of amyotrophic lateral sclerosis and critical nutritional impairment:

- Rapid progression: independent ambulation to wheelchair or bed-bound status
- Progression from normal to barely intelligible speech
- Progression from normal to pureed diet
- Needing major assistance by caretaker in all activities of daily living

2B. Critical nutritional impairment as demonstrated by all of the following:

- Oral intake of nutrients and fluids insufficient to maintain life
- Continuing weight loss
- Dehydration or hypovolemia
- Absence of artificial feeding methods sufficient to sustain life but not for relieving hunger

3. Patient should demonstrate both rapid progression of amyotrophic lateral sclerosis and at least 1 life-threatening complication:

- Recurrent aspiration pneumonia
- Decubitus ulcers
- Recurrent fever after antibiotics
- Inability to maintain sufficient fluid and caloric intake with 10% weight loss during past 6 months or serum albumin lower than 2.5 g/dL

Specific information may be found at <http://www.umd.nycpic.com/cgi-bin/bookmgr/bookmgr.exe/BOOKS/M984/?FRONT>

ceived values and beliefs. Meier and Morrison⁸² noted editorially, “When desperately ill patients and their families opt for desperate treatments, they should also be asked under what circumstances death would be preferable to life with severe impairment and whether treatments should be discontinued if those circumstances occur.”

In brief, the overriding advantages are that LTMV secures the airway, prevents or reduces aspiration pneumonia, and by providing automated mechanical breathing, prolongs life (Box 1).¹⁵ Some patients continue to feel that life has purpose and meaning, and they can engage in social, religious, recreational, intellectual, and other activities even when they lose all mobility and can move nothing except their eyes.^{70,83}

One of our patients continued to go to the opera in her power wheelchair and portable machine, along with her 24-hour registered nurse, although she was totally paralyzed and mute. Communication remains feasible for varying amounts of time, using laser-assisted pointers with computers, alphabet boards, and other assistive devices. In late stages, “yes” and “no” can be signaled with eye gaze or blinks.³⁶

Disadvantages concern both the patient and family caregivers. Although the patient is alive, the disease progresses relentlessly. With LTMV, frequent (in some cases hourly) mechanical suctioning to remove secretions is essential, and it can cause gagging and distress. The costs of home care are immense, and family responsibilities and burdens are great. Caregivers of patients dependent on invasive ventilator assistance report substantial levels of distress, and, in the few studies of this population, caregivers were more likely than patients to express regret about having chosen LTMV.^{70,84}

Ideally, the patient, family, and physician have discussed end-of-life issues and preferences, and the patient’s wishes are known well in advance of a crisis.⁸¹ SP provides a best-case scenario. He has formulated a plan and has told his family and his physician how he wants his death to occur. He has chosen not to pursue tracheostomy and LTMV.

The frequency with which withdrawal of LTMV occurs is unknown. Some patients may ultimately require palliative sedation.⁸⁵ For patients who withdraw LTMV or choose not to have it, palliation becomes the sole focus of interventions, including treating pain and managing other symptoms, such as dyspnea, fear, anxiety, sialorrhea, and constipation.

End-of-Life Care and Referral to Hospice

DR SP (THE PATIENT): *When I become dependent on BiPAP (non-invasive ventilation or NIV) most of the day and night, one night I will go to bed without the BiPAP on and have family around me.*

TP (THE PATIENT’S WIFE): *It sounds easy, but I don’t know how easy that’s going to be.*

Discussing the fatal nature of ALS and end-of-life decision making with patients and families is not easy. Although the general issues are best raised soon after diagnosis, the actual decision regarding hospice should be faced before respiratory capacity declines substantially. BOX 3 summarizes triggers that can lead to discussion of these issues. BOX 4 presents the Medicare criteria for hospice referral.

Home hospice is particularly helpful for ALS patients in late-stage illness because most are essentially housebound due to loss of mobility, and the multiple services hospice provides at home would not otherwise be available.⁸⁶ However, home hospice is not generally an option for patients who have decided to seek tracheostomy or LTMV or who have no informal caregiver living with them.

Wish to Die and Hastened Death

Patients with ALS may be more likely to consider a hastened death than other patients,⁸⁷ although the large majority neither request nor act on such a consideration. Has-

tened death may be more closely associated with weariness, suffering, or a loss of meaning and purpose in life than clinical depression,⁸⁸ although this has not been systematically determined. In a prospective study of patients in the late stages of ALS, Albert et al⁸⁹ found that although 10 of 53 patients (19%) who died during the period of observation had previously expressed a wish to die, only 3 (6%) actually arranged for a hastened death. Hastened death is distinguished from refusal of LTMV and respiratory failure, which also results in death, in that it refers to a specific request by the patient to arrange for a death that is not otherwise imminent, including physician-assisted suicide. According to Ganzini and Johnston,⁹⁰ about 3% of all ALS deaths are by assisted suicide. ALS is the most common diagnosis among patients who die with physician-assisted suicide in Oregon, where it is legal.⁹¹ Paradoxically, however, among other terminally ill patients, such as those with AIDS, sometimes sanctioning a patient's right to choose the timing of an inevitable and foreseeable death helps to sustain them and to extend the duration of their willingness to live.⁹²

CONCLUSIONS

Chronic neurodegenerative disorders, such as ALS, are among the most difficult diseases with which clinicians must deal. These diseases, and ALS in particular, take a predictable terminal course, impairing verbal communication, oral intake, and respiration. The deterioration is often too fast for the patient and family to adjust well to these changes. To deliver the diagnosis of this well-publicized disease requires great sensitivity and care. Sooner rather than later, the clinician must discuss the nature of the disease and the importance of advance directives, always striving to maintain realistic hopes. Even as death approaches, a multidisciplinary strategy should be used, assisting family caregivers who play a central role in patient management. Thus, the physician caring for patients with ALS experiences both extraordinary burdens and extraordinary opportunities in providing expert care throughout this tragic illness.

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Other Sources: For a list of Web sites and patient recommendations, see the article on the JAMA Web site at <http://www.jama.com>.

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Web Resources for Amyotrophic Lateral Sclerosis

Patient Guides

Mitsumoto H, Munsat TL, eds. *Amyotrophic Lateral Sclerosis. Patient and Family Guide to Management and Care*. 2nd ed. New York, NY: Demos; 2001. <http://www.demosmedpub.com>. (800) 532-8663.

Miller RG, Gelinas D, O'Connor P. *Amyotrophic Lateral Sclerosis*. New York, NY: Demos; 2004. <http://www.demosmedpub.com>. (800) 532-8663

Everyday Life With ALS: A Practical Guide. Tucson, AZ: Muscular Dystrophy Association; 2005. <http://www.alsmdausa.org>

WEB SITES FOR PATIENTS AND FAMILIES

Muscular Dystrophy Association

<http://www.mda.org>

The Muscular Dystrophy Association is a national voluntary health agency dedicated to conquering more than 40 neuromuscular diseases. It provides information about the ongoing medical research and fundraising efforts and includes an amyotrophic lateral sclerosis (ALS) division.

ALS Association

<http://www.alsa.org>

This Web site provides information about community organizations and public policy related to ALS, includes information for all those affected by ALS—patients, families, caregivers, and health care professionals, and discusses current research and donation opportunities.

Family Caregiver Alliance

<http://www.caregiver.org>

An advocate for caregivers, the Family Caregiver Alliance offers information, education, and support to those caring for loved ones with chronic, disabling illnesses. It also provides information on research and advocacy.

National Alliance for Caregiving

<http://www.caregiving.org>

The National Alliance for Caregiving is a nonprofit coalition of national organizations focusing on issues of family caregiving. It offers support to family caregivers and the professionals who help them, and it includes caregiving tips and information on events.

National Family Caregivers Association

<http://www.nfcares.org>

This association educates, empowers, and supports those who care for a loved one with a chronic illness or disability, addresses the common needs and concerns of family caregivers, and offers the opportunity to join a caregiving network.

CareGuide

<http://www.careguide.com>

This Web site offers innovative solutions to improve health and financial outcomes by matching people with the proper service and by combining technology with optimum human contact. The organization's goal is to assist

patients and families in making the best health care decisions.

ElderCare Online

<http://www.ec-online.net>

This site provides information, education, and support to people caring for aging loved ones in an effort to improve quality of life for the caregiver as well as the elder.

Today's Caregiver

<http://www.caregivers.com>

Today's Caregiver offers information, support, and guidance for family and professional caregivers.

Social Security Disability Planner

<http://www.ssa.gov/dibplan/index.htm>

The Social Security Disability Planner explains benefits to those who are disabled, defines how individuals can qualify for benefits, outlines the application process, and details who can receive benefits based on one's earnings record.

Medicare Rights Center

<http://www.medicarerights.org>

The Medicare Rights Center provides health care information and assistance for people who receive Medicare benefits; helps older adults and people with disabilities receive good, affordable health care; addresses the common needs and concerns of family caregivers; and offers individuals the opportunity to join a caregiving network.