



## Management of Patients With Amyotrophic Lateral Sclerosis

**A**myotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease—affecting motor control neurons in the spinal cord, brain stem, and motor cortex—resulting in muscle weakness and atrophy, and corticospinal tract signs, such as hyperactive tendon reflexes, clonus, spasticity, and a positive Babinsky sign. Death from respiratory failure (a complication of ALS) usually occurs within 3 to 5 years of symptom onset.<sup>1</sup>

Initial symptoms of ALS are often subtle and asymmetric, involving clumsiness of fine hand function, finger stiffness, hand weakness, and atrophy. With time, other upper-limb muscles, including the shoulder girdle musculature, are affected. Typically, atrophic weakness spreads upward to the neck and bulbar musculature, and downward to the trunk and lower limbs. Lower-extremity spasms and cramps often occur at night and following exercise. The common functional problems associated with ALS include impaired hand function and mobility, and dysphagia and dysarthria. Additional impairments include nutritional deficiency due to dysphagia, sialorrhea, respiratory dysfunction, difficulty toileting, and pain.

### EPIDEMIOLOGY

Sporadic ALS is an adult-onset, neurodegenerative disorder of unknown etiology. The illness is rare before age 40 years, with the risk increasing with age thereafter. Men are at higher risk than women, with a ratio of 1.3:1.<sup>2</sup>

**Ms. Banks** is a program coordinator and analyst, and **Dr. Ruff** is the national chief of neurology services, both at the Louis Stokes Cleveland VA Medical Center in Ohio.

Epidemiologic studies have identified associations of sporadic ALS with work in occupations that involve exposure to toxins. Familial ALS (FALS) is usually autosomal dominantly inherited.<sup>3</sup>

### INFLUENCE OF MILITARY SERVICE ON THE RISK OF DEVELOPING ALS

A study by the Institute of Medicine (IOM) concluded that, “there is limited and suggestive evidence of an association between military service and later development of ALS.”<sup>4</sup> Data from the study indicated that locality of service and history of combat exposure did not clearly influence the incidence of ALS. In addition, the IOM report noted that the annual incidence of ALS among adults over age 18 years is between 2.5 to 3.0 per 100,000 people.<sup>4</sup> The likelihood of a person dying from complications associated with ALS is increased 1.5-fold if that individual is a veteran, however. The IOM report did not define factors that underlie the increased veteran incidence of ALS because of the overall low incidence of this disease.

### DIAGNOSIS

Patients with suspected ALS should be evaluated by an experienced clinician.<sup>5,6</sup> ALS varies considerably among individuals regarding the pattern of onset and rate of progression.<sup>7-9</sup> A diagnosis of ALS should be confirmed or excluded as quickly as possible, in order to avoid unnecessary diagnostic testing, to initiate neuroprotective medication in a timely manner, and to allow the patient a greater amount of quality time to better plan the remaining segment of his/her life.

### Diagnostic workup

A comprehensive diagnostic workup should include: history and physical examination, including a thorough neurologic examination; electrodiagnostic tests, including electromyography and nerve conduction velocity; blood studies with high-resolution serum protein electrophoresis; evaluation of thyroid and parathyroid hormone levels (in cases with minimal spasticity, anti-GM1 antibody titres are indicated to rule out a diagnosis of anti-GM1 antibody syndrome); and urine studies, including 24-hour

The VHA's Specialty Care Services includes medical services with a wide range of subspecialties; emergent and urgent care and patient support services, such as nutrition; spiritual care and other specific-purpose programs, such as cancer registry and Centers of Excellence for multiple sclerosis, epilepsy, and Parkinson disease. The Office of Specialty Care Services brings you “Updates in Specialty Care,” sharing the latest evidence-based approaches, each column featuring a different topic and providing updates on existing programs, and introducing new programs. Special thanks to Margaret (Maggi) Cary, MD, MBA, MPH, director of the VA's Physician Leadership Development Program, who coordinates and edits the column. Please send suggestions for future columns to [margaret.cary@va.gov](mailto:margaret.cary@va.gov).



urine collection for heavy metals in patients who do not have definite corticospinal tract signs. Lumbar puncture sometimes is indicated to exclude a demyelinating polyradiculopathy. Radiographic studies, including magnetic resonance imaging or myelogram of the cervical spine, should be considered in cases in which the corticospinal signs and upper-extremity weakness and wasting can be explained by a cervical spinal cord condition, such as cervical spondylitic myelopathy. Muscle and/or nerve biopsy may be necessary to exclude the possibility of multifocal motor neuropathy.

Repetition of the investigations may be needed if the initial series of tests does not result in a definitive diagnosis.<sup>5</sup> A person who receives a diagnosis of ALS should be encouraged to seek a second opinion from an ALS expert. Neuromuscular disease specialists are the optimal clinicians to provide this level of expertise in diagnosis and care.<sup>10</sup> Review of the diagnosis is advisable if there is no evidence of progression or if the patient develops atypical features.<sup>5</sup>

### **Communicating the diagnosis**

Patients often are dissatisfied with how the ALS diagnosis was communicated.<sup>5</sup> The diagnosis should be communicated in person, in a direct, understandable, empathetic, sensitive, and supportive manner; by a clinician with good knowledge of the patient and ALS.<sup>5,6</sup> The clinician should allow ample time (at least 45 to 60 minutes) and begin by asking what the patient already knows or suspects.<sup>5</sup> The diagnosis and its implications should be discussed in a step-wise fashion, checking repeatedly to ensure that the patient understands what is being said.<sup>5</sup> The cultural and social background of the patient should be respected by asking whether the patient

wishes to receive information solely or if he/she would like to include another person in the discussion.<sup>5</sup>

The complex service needs of patients with ALS are best addressed when 1 physician oversees and integrates the interdisciplinary care of the patient. This physician serves as the liaison between specialty services and the primary care medical providers for the patient. Printed materials about the disease, about support and advocacy organizations, and about informative Web sites on the Internet should be provided. A letter or audiotape, summarizing what the physician has discussed, also can be very helpful for the patient and family.<sup>5</sup>

The clinician should reassure the patient and his/her family that they will not be abandoned, but, rather, that they will be supported by a professional ALS care team and with regular follow-up visits, as needed.<sup>5</sup> The clinician should avoid withholding the diagnosis, providing insufficient information, delivering information callously, or abolishing hope.<sup>5</sup>

### **MANAGEMENT OF ALS**

#### **Advantages of an experienced multidisciplinary team**

Experienced multidisciplinary teams are highly advantageous in caring for patients with ALS. The team may include: an ALS physician (neurology, physical medicine and rehabilitation, or internal medicine), primary care provider (by telehealth or teleconference, if necessary), palliative care or hospice care team staff member, speech-language pathologist, physical therapist, occupational therapist, pharmacist, psychologist (clinical health psychologist), dietitian, pulmonologist, respiratory therapist, gastroenterologist, nurse, social worker, therapeutic recreation specialist, assis-

tive technology specialist, and a chaplain from the patient's preferred faith or religion. Connection with an ALS-related organization also is beneficial and can enable the patient and family to exchange information with others who have ALS.

### **Clinical care**

The major focus of clinical care is to provide the highest quality of life through management of emotional and physical symptoms. The care team should determine early in the course of treatment the patient's wishes for feeding and whether he/she would want a tracheostomy and mechanical ventilation.<sup>5</sup> It is critical that the patient determines how he/she will live.

For patients who chose not to have a tracheostomy, the discomfort of dyspnea can be treated using opioid medication alone or in combination with benzodiazepines if anxiety is present.<sup>5</sup> Pain should be addressed earnestly with opioids, if needed. When withdrawing ventilation, the use of adequate opiates and anxiolytics are essential to relieve dyspnea and anxiety.

Quality-of-life instruments can detect issues that should be addressed in order to improve the end of life.<sup>10</sup> The care team should inform the patient about advance directives and the naming of a health care proxy, offer assistance in formulating an advance directive, and repeat the discussion of the patient's preferences for life-sustaining treatments with any change in his/her condition.<sup>5</sup>

Management of care should balance the need for accessible local care with the need for interdisciplinary ALS specialty care.<sup>11</sup> The symptoms most likely to be encountered by patients with ALS at some point in their lives include difficulty communicating (62%), dyspnea (56%), insomnia (42%), pain (30% with severe

or constant pain), discomfort other than pain (48%), choking (52%), depressed mood (40%), anxiety (30%), confusion (10%) and, on a rare occasion, frontal lobe dementia.<sup>12</sup>

### Pharmacologic treatment

Riluzole is the only pharmacologic treatment that has been demonstrated to prolong life by a few months. Riluzole slows ALS progression, by reducing levels of glutamate—a chemical messenger in the brain that often is elevated in people with ALS. Currently,

is the most common feeding intervention for ALS patients. In cases where the above interventions have failed to control reflux and aspiration, a jejunostomy tube may be inserted to eliminate the risk of aspiration.

As muscle weakness progresses, the diaphragm and chest wall are unable to function effectively and pulmonary toileting is essential. Interventions used to enhance pulmonary toileting may include, but are not limited to, controlled-breathing exercises, assisted coughing techniques,

the standard 5-day consult processing requirement. Given the volume and complexity of AT devices that will be utilized by the patient with ALS, and the need to interface multiple electronic devices for varied environments of use, it is strongly recommended that services be coordinated by a skilled AT professional.

### Social issues

Approximately 61% of patients with ALS die at home.<sup>10</sup> To enhance end-of-life care, social issues, such as death and dying, should be addressed early, including referral to hospice or home care.<sup>5</sup> A liaison with local pastoral care workers should be established to address the spiritual needs of the patient and relatives.<sup>5</sup> Health practitioners need to accept the patient's spiritual and religious attitudes, while remaining committed to relieving his/her suffering.<sup>10</sup> Bereavement support should be offered to the patient and his/her family and caregivers. After the patient dies, the care team should send letters of condolence to the family.<sup>10</sup>

### CONCLUSION

ALS became a presumptively compensable illness for all veterans with 90 days or more of continuously active service in the military. As a result, the VA Health Care System (VAHCS) created a national registry of veterans with ALS to track their health status and to help recruit research participants. The location of care is dictated by the needs of the veterans with ALS. Care generally takes place as close to home as possible and is delivered in a variety of settings and methods, including telehealth. However, regardless of the location, if ALS is the primary or a secondary diagnosis, it is recommended that providers of ALS care be made aware of the veteran's enrollment into the VA system.

Overall, ALS care at the VA is comprehensive, interdisciplinary, and co-

*To enhance end-of-life care, social issues, such as death and dying, should be addressed early, including referral to hospice or home care.*

the exact mechanism behind the neuroprotective properties in human ALS has not been indisputably elucidated, but includes antigitamatergic actions, Ca<sup>2+</sup> and Na<sup>+</sup> channel blockade actions, GABAergic mechanism, and interactions with various intracellular proteins in neuronal membrane receptors to extend neuron life.<sup>13</sup> Adverse effects associated with riluzole are asthenia and nausea. Riluzole is contraindicated in ALS patients with active liver disease or an elevated level of transaminase.<sup>14</sup>

### Feeding and pulmonary toileting

Because of the increased risk of airway obstruction from aspiration in ALS patients, feeding tubes often are used. For short-term use, a nasogastric tube may be placed. A longer-term solution is an esophageal tube, which is placed through an opening in the side of the neck and inserted into the stomach. Percutaneous endoscopic gastrostomy

suctioning via tracheotomy, and use of an in-exsufflator. The incentive spirometer is also an important adjunct and should be used every 1 to 2 hours while the patient is awake.

### Durable medical equipment

Given the limited life expectancy of patients with ALS, there is a need to expedite provision of assistive technology (AT) and durable medical equipment. This requires coordination with the prosthetic and sensory aids services (PSAS). Low-tech devices should be available as “stock” for same-day provision. Low-tech devices include, but are not limited to, aids for dressing, bathing, grooming, eating, and drinking; ambulation aids, including standard wheelchairs and wheelchair cushions; and off-shelf orthotic devices. For nonstock items, the PSAS consult processing time should be reduced to 1 working day for ALS clients, compared with

managed among primary care providers and the ALS team. Care is delivered as efficiently as possible from the perspective of the veteran with grouping of clinic appointments, minimization of travel to the care setting, and expedient delivery of durable medical equipment. ALS care within the VAHCS is predominately outpatient-based with periodic admissions. Presently, approval of an ALS handbook, which will standardize the care process of ALS throughout the nation, is pending. In summary, the VHA's Specialty Care Services provide a seamless delivery of specialized health care, continuous educational and consultative support, research, and community resources for veterans with ALS while increasing access to care and education for the patient, their caregiver, and their families.

**Author disclosures**

The authors report no actual or potential conflicts of interest with regard to this column.

**Disclaimer**

The opinions expressed herein are those of the authors and do not necessarily reflect those of Federal Practitioner, Quadrant HealthCom Inc., the U.S. Government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.

**REFERENCES**

1. Mitsumoto H, Hanson MR, Chad DA. Amyotrophic lateral sclerosis. Recent advances in pathogenesis and therapeutic trials. *Arch Neurol.* 1988;45(2):189-202.
2. Nelson LM. Epidemiology of ALS. *Clin Neurosci.* 1995-1996;3(6):327-331.
3. Majoor-Krakauer D, Willems PJ, Hofman A. Genetic epidemiology of amyotrophic lateral sclerosis. *Clin Genet.* 2003;63(2):83-101.
4. Institute of Medicine of the National Academies' Committee on the Review of the Scientific Literature on Amyotrophic Lateral Sclerosis in Veterans. *Amyotrophic Lateral Sclerosis in Veterans: Review of the Scientific Literature.* Washington, DC: The National Academies Press; 2006.
5. Andersen PM, Borasio GD, Dengler R, et al. EFNS task force on management of amyotrophic lateral sclerosis: Guidelines for diagnosing and clinical care of patients and relatives. *Eur J Neurol.* 2005;12(12):921-938.

6. Chio A. ISIS Survey: An international study on the diagnostic process and its implications in amyotrophic lateral sclerosis. *J Neurol.* 1999;246(suppl 3):III1-III5.
7. Brooks BR. El Escorial World Federation of Neurology criteria for the diagnosis of amyotrophic lateral sclerosis. Subcommittee on Motor Neuron Diseases/Amyotrophic Lateral Sclerosis of the World Federation of Neurology Research Group on Neuromuscular Diseases and the El Escorial "Clinical limits of amyotrophic lateral sclerosis" workshop contributors. *J Neurol Sci.* 1994;124(suppl):96-107.
8. Munsat TL, Andres PL, Finison L, Conlon T, Thibodeau L. The natural history of motoneuron loss in amyotrophic lateral sclerosis. *Neurology.* 1988;38(3):409-413.
9. Ringel SP, Murphy JR, Alderson MK, et al. The natural history of amyotrophic lateral sclerosis. *Neurology.* 1993;43(7):1316-1322.
10. Mitsumoto H, The ALS Peer Workgroup Members. *Amyotrophic Lateral Sclerosis: Completing the Continuum of ALS Care: A Consensus Document.* Missoula, MT: The University of Montana Press; 2004.
11. Miller RG, Rosenberg JA, Gelinas DF, et al. 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: ALS Practice Parameters Task Force. *Neurology.* 1999;52(7):1311-1323.
12. Ganzini L, Johnston WS, Silveira MJ. The final month of life in patients with ALS. *Neurology.* 2002;59(3):428-431.
13. Cheah BC, Vucic S, Krishnan AV, Kiernan MC. Riluzole, neuroprotection and amyotrophic lateral sclerosis. *Curr Med Chem.* 2010;17(18):1942-1959.
14. Bensimon G, Doble A. The tolerability of riluzole in the treatment of patients with amyotrophic lateral sclerosis. *Expert Opin Drug Saf.* 2004;3(6):525-534.

## CALL FOR REVIEWERS

Federal Practitioner welcomes applications from physicians, pharmacists, nurse practitioners, and physician assistants interested in participating in the peer-review process. While professionals in all areas of patient care and pharmaceutical practice are encouraged to apply, at this time Federal Practitioner is particularly interested in reviewers with expertise in the following specialty areas:

- Cardiology • Critical care • Endocrinology • Gastroenterology • Oncology  
• Research: Design, ethics, statistical analysis • Sleep disorders • Urology**

To apply, please e-mail a copy of your CV and a letter describing all subject areas of interest to [fedprac@qhc.com](mailto:fedprac@qhc.com) or mail them to: Editor, Federal Practitioner, Quadrant HealthCom Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609.