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Amyotrophic Lateral Sclerosis and the Need for Cultivating Advocacy Urgency

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Introduction

Amyotrophic lateral sclerosis (ALS) was identified well over a century ago as a motor neuron (affecting both upper and lower) disease. This disease impairs voluntary muscle movement and control leading to debilitating consequences in activities of daily living.[1] It was given the moniker "Lou Gehrig's Disease" after the namesake American professional baseball player ultimately succumbed to complications of the condition in 1941, less than two years after he was diagnosed.[2] Muscles that can no longer be used, begin to atrophy and harden. Consequently, affected individuals lose the ability to perform life-enhancing activities like speaking and moving, and life-sustaining activities like eating and breathing. Respiratory system compromise and ventilatory failure eventually occur in most, if not all, patients as the disease progresses.[3] ALS is considered a rare disease because it affects fewer than 200,000 Americans. According to the National Organization for Rare Disorders[4], approximately 30,000 people are affected in the U.S. with 5,000 new diagnoses each year. It has an incidence rate of 1.5 to 3 per 100,000 people in both North American and European populations, which is where most of our epidemiologic research stems.[4] Despite the disease's documented rarity, the impact it has on the person with ALS (pALS) is unquestionable. This editorial explores components of the disease state that highlight the urgency of cultivating enhanced advocacy efforts, primary legislative acts that have been approved and are being requested, and how individuals and organizations can become involved in these herculean endeavors.

Symptomology

An examination of the symptoms related to ALS further highlights the disease's impact, not only on those diagnosed but, on the individual's loved ones and caregivers. Progressive muscle weakness, increased or decreased muscle tone and reflexology depending on the motor neurons affected, muscle cramps, fasciculations/twitching, falls secondary to foot drop, dyspnea, and difficulty speaking/swallowing are all notable complaints.[4] The ladder symptoms can then lead to aspiration and pneumonia which could expedite respiratory failure. These symptoms may begin as subtle and asymmetric, yet progress to being crude and widespread. Additional signs and symptoms of ALS can be characterized as non-motor and affect up to half of the disease population.[4] These include reduced cognitive function, pseudobulbar affect (PBA), and frontotemporal dementia (FTD). Huynh et al.[5] found a higher likelihood of reduced cognitive function in those with respiratory compromise. Pseudobulbar affect presents as emotional lability, which could include sudden episodes of inappropriate or uncontrollable laughing or crying.[4]These episodes are often out of proportion with the associated (if any) trigger or situation.[6] Pseudobulbar affect can be difficult to distinguish from depression in some cases. Frontotemporal dementia can also result in mood alterations such as disinhibition and compulsory behavior. The burden of these symptoms coupled with the fear of death has led to a statistically worse reported quality of life in pALS and their caregivers.[7]

Time to Diagnosis

The path to an ALS diagnosis can be quite challenging. Due to its complexity and un-commonality, some healthcare providers may not be familiar with its clinical presentation or it simply mimics other neurological conditions. Some pALS report non-specific, pre-clinical symptoms [predromal stage] years before the diagnosis is confirmed.[8] This diagnostic delay can result in the further deterioration of functionality, with missed benefits and opportunities for early intervention. From the onset of seeking medical consultation for symptoms to diagnosis, can take up to 16 months.[9-10] There is no specific blood test or biomarker that lends to the diagnosis, thus we must rely on supportive testing which can include electromyography (EMG), nerve conduction studies (NCS), magnetic resonance imaging (MRI), lumbar puncture (LP), and muscle biopsies. Not only can this testing be expensive and time-consuming, but in some cases- painful. Like

with any disease or condition, early identification and intervention are necessary to have positive outcomes. We could potentially modify the disease's course and "buy more time" in the way of treatment developments. The sooner we can reach a diagnosis, the better placement the pALS is if they wish to enroll in clinical trials.[11] We must prepare those affected for the plan of care that works best for them, not prolong the inevitable after due diligence has been observed.

Role of Genetic Testing

Though the majority of ALS cases have no known cause, approximately 10% can be considered familial or inherited. This means that a mutated gene has been passed down in the bloodline. While this is unfortunate, it does open the door for genetic testing to serve as a biomarker of sorts which could lessen the timeframe for diagnosis in these instances.[9] The most common mutated genes associated with ALS are *SOD1* and *C9orf72*, which have only been discovered over the last three decades. Interestingly, both the aforementioned genes can occur in sporadic cases of ALS too. There are now over 40 genes that account for the majority of familial ALS cases. *C9orf72* can also lead to the development of FTD. Whether genetic testing is used as predictive or confirmatory, this option is not without its hurdles. First, it can be a difficult decision to make due to the psychological burden that can be placed on the recipient. It is a very personal decision, yet it could impact many in terms of familial risk. A positive test might help determine progression while a negative test does not eliminate the chance of disease development. Predictive testing requires several "hoops to jump through" (neurologic exam, psychological assessment, genetic counseling) before being approved. Second, genetic testing can be expensive, even with health insurance coverage and physician recommendations. In addition to knowing the "why" behind a diagnosis, genetic testing can also help to identify gene-targeted therapy that may apply to their respective case. Currently, only increased age and family history are known risk factors for the condition.[4] A recently published evidence-based consensus guideline recommends that all persons with ALS should be offered genetic testing with a panel that includes *C9orf72, SOD1, FUS, TARDBP*, and any gene in which there is a Food and Drug Administration (FDA)-approved targeted therapy.[12] With further adoption, these guidelines will establish a clinical standard of care for genetic testing in pALS and greater access to valuable members of the multidisciplinary care team.

Navigating Insurance Demands

The struggles identified in the preceding section, segue nicely into another area of frustration experienced by both the pALS and the providers who are assessing for and recommending treatment options- insurance. If the affected pALS is still working, they likely have employer-sponsored coverage and if over the age of 65, likely have Medicare benefits. When the individual is military-connected, health benefits can be provided through Veterans Affairs (VA). If the person does not work or is no longer able to, Social Security Disability benefits can be sought. There are two primary barriers associated with insurance: access to the needed care and denials for recommended treatment or equipment. Questions that pALS and their caregivers should ask include: Is durable medical equipment (DME) covered by my plan? Are ALS-specific drugs covered by my plan? Is home health covered? Will I have access to palliative or hospice care? The ALS Association has an evidence-based resource guide called 'The Case for Coverage' which helps educate and empower advocates to move the needle for broader access and quicker approval for life-prolonging medication and equipment.[13] The need for prior authorization and limiting approval to later in the disease's progression are the primary causes for this delay in access. Though we don't want to over-prescribe, we also are keenly aware of how early intervention can increase longevity. The time it takes to document and file appeals can result in further pALS deterioration. Traditionally, for those who pursue Social Security Disability Insurance (SSDI) before the age of 65, there is a two-year Medicare

waiting period before access to that coverage is granted. Thankfully, since 2001 through the work of advocacy, those diagnosed with ALS have this waiting period waived and Medicare entitlement begins simultaneously with disability benefits.[14] This is a prime example of effective advocacy and placing the interests of patients above the red tape.

Access to Multidisciplinary Care

Due to the pervasiveness of symptoms in ALS, a variety of healthcare providers can offer the needed support and guidance to identify recommended treatment and therapy options. The multidisciplinary team often consists of neurologists, respiratory therapists, occupational therapists, physical therapists, speech-language pathologists, dietitians, social workers, nurses, and various allied health professionals who specialize in neuromuscular disease.[15] Having all these providers in one place, at one time in a dedicated clinic decreases the time and travel for pALS seeking care. In a practice parameter update, Miller et al.[16] recommend multidisciplinary ALS clinic management to optimize the delivery of healthcare services, prolong the pALS's survival, and enhance their quality of life (QoL). There are a multitude of benefits to attending a multidisciplinary clinic. The patient and their family are at the center of every evaluation and recommendation through a shared decision-making process. This continuity and coordination of comprehensive care leads to greater patient satisfaction.[15] There are over 200 multidisciplinary ALS-certified centers and clinics in the U.S. The ALS Association distinguishes the types of centers by the services they offer which include a Certified Treatment Center of Excellence, a Recognized Treatment Center, an Affiliated Clinic, and those associated with the Veterans Administration. While this number is encouraging, some pALS would still need to travel several hours to attend this type of clinic in person. In light of this, many clinics now offer a telehealth option. Though the concept of telehealth is not new, the COVID-19 pandemic highlighted its direct importance and applicability in chronic disease management. Not only can this virtual-based healthcare delivery medium help overcome logistical challenges, but it has also been shown to enhance collaboration with primary care and community-based clinical partners, allow for the setting and monitoring of noninvasive ventilation (NIV), increase utilization of vital services, and maintain the pALS's functional status.[17] Both patients and clinicians must be amendable to this practice and decide early on how this mode of healthcare delivery will be used following the initial in-person consultation.

Research and Clinical Trials

As a community, we have made great strides in ALS-specific research. The first FDA-approved agent was riluzole which has been available since 1995. It comes in three formulations: oral pill, thickened liquid, and oral film. In the last decade, scientists have discovered and developed two new pharmacologic agents. Edaravone, which can be administered intravenously or orally, and the first genetically targeted therapy, tofersen, which treats *SOD1*-ALS.[18] With ALS being a service-connected disease, the Department of Defense appropriated $5 million in 2007 to fund an ALS Research program (ALSRP). This funding has been as high as $41 million in 2022.[19] The ALSRP focuses on developments in therapeutics, biomarkers, and clinical trials for new and existing therapies. In 2010, the Centers for Disease Control and Prevention (CDC) inaugurated the National ALS Registry wherein pALS could self-report data allowing researchers a broad platform from which to study and curate statistics. Subsequently, the National ALS Biorepository was created which collects, stores, and shares donated blood and saliva samples for research purposes to better understand the unique causes of the disease.[20] Funding from the National Institute of Neurological Disorders and Stroke (NINDS), a subdivision of the National Institutes of Health (NIH), has also increased funding for ALS-specific research to $219 million in 2023.[21]

Legislative Acts & Advocacy

An advocate informs, supports, and recommends policy change. Probably the most well-known ALS advocacy effort was the Ice Bucket Challenge which

originated in 2014. The ALS Association reports 17 million recordings of the challenge, spanning 159 countries, 10 billion views, and a staggering 220 million dollars raised.[22] In the decade since we have had two new treatment options, doubled the number of multidisciplinary clinics, discovered several new ALS genes, and increased both support and funding from state and federal government agencies. This level of advocacy has impacted research opportunities, policy change, and the lives of those living with ALS. It's important to reflect on and celebrate our advocacy's 'wins'.

- The Genetic Information Nondiscrimination Act (GINA) of 2008 prohibits third-party payers and employers from discriminating based on the results of genetic testing (i.e. higher premiums, being dropped from coverage, and/or loss of employment).[23]
- The ALS Disability Insurance Access Act of 2019 (H.R. 1407/S.578) eliminated the five-month waiting period for disability benefits. Before this became law in 2020, pALS had to wait for those five months after becoming and being documented as disabled before benefit payments would begin.[24]
- The Accelerating Access to Critical Therapies (ACT) for ALS Act (H.R. 3537) became law in 2021 which requires the Department of Health and Human Services (HHS, NIH, and FDA) to establish grants for the research and development of treatments for ALS.[25]

In the same vein, we must look toward what we can accomplish next. The following are acts/bills that are still under consideration and should be the continued focus of ALS advocates.

- The Genetic Testing Protection Act is a state-initiated request to extend genetic testing protections to other types of insurance including, life, long-term care, and disability. Maryland, New York, Illinois, and Tennessee are considering this change to public policy. State legislation often moves quicker than federal, but it can also inform future policies for federal adoption once they have been shown impactful.[26]
- The Benefit Act (S.526/H.R.1092) of 2023 would help ensure transparency from the FDA during the approval process and would allow for the consideration of patient-reported experience data when weighing the risks and benefits of a proposed therapy.[27]
- The Justice for ALS Veterans Act (H.R. 3790/S. 1590) would extend dependency and indemnity compensation (DIC) to the surviving spouse of a veteran who succumbs to ALS regardless of how long the individual had the disease before passing. This benefit has historically only been available to those who have experienced eight years of disability.[28] The average lifespan after diagnosis of ALS is two to five years.
- The Promising Pathway Act (H.R. 4408/S.1906) of 2021 seeks to establish a provisional and priority (i.e. expedited) approval pathway for medicines that are intended for life-threatening diseases (such as ALS) that cannot be denied by health insurers based on the agent being experimental or provisionally approved.[29]
- In 2023, the bipartisan bill known as the 'Expanded Telehealth Access Act' (H.R.3875/S.2880) was introduced in the Senate which would allow vital members of the multidisciplinary team, including PTs, OTs, and SLPs, to provide telehealth services under Medicare outside the bounds of a public health emergency.[30]
- The Elizabeth Dole Home Care Act (H.R. 542/S.141) of 2023 would require the VA to provide enhanced medical and social services to veterans who wish to remain at home during their battle with ALS, improve home care support for caregivers, and raise the limit on nursing home care assistance provided outside VA facilities.[31]
- The Healthy Brains Act (H.R. 9233) of 2024 stands for *Harmonizing Environmental Analyses and*

Launching Therapeutic Hubs to Yield Bolstered Research And Innovation in Neurological Science and urges the NIH to create Collaborative Centers for Neurodegenerative Disease Environmental Research to identify environmental risks associated with neurodegenerative diseases like ALS.[32]

- The EDUCATE Act (H.R. 7725) of 2024 stands for *Embracing Anti-Discrimination, Unbiased Curricula, and Advancing Truth in Education* and would decrease/eliminate federal funding to any medical school that has diversity, equity, and inclusion programs. Advocates are urging opposition to this act so that any person diagnosed with ALS would have equal access to the care and clinical trials to which they are entitled.[33]
- The ALS Better Care Act (H.R. 5663/ S.3258) would provide greater payment (i.e. Medicare reimbursement) for ALS-related providers in a multidisciplinary clinic setting. This supplemental payment could help increase access to the gold standard of ALS care, decrease preventable costs and wait times, and improve survival rates/outcomes. If approved, it would be enacted on January 1, 2025.[34]

As you can see, there are numerous federal and state public policy priorities for which individuals and organizations who wish to support those affected by ALS can become involved. Advocacy begins with an awareness of the enormity of the problem, which the author hopes has been adequately conveyed. The knowledge that time is fleeting for those impacted by this rare disease and that funding is not sufficient should generate a sense of urgency in society and in those with whom we elect to make vital legislative decisions. Contacting members of the ALS Congressional Caucus is a great place to start as they are the disease's bipartisan governmental 'champions'.[35] Likewise, the CDC has a list of organizations that support ALS patients and their caregivers.[36] In 2022, the NIH commissioned a National Academies committee of experts to develop a 'roadmap' or key actions to make ALS a more livable disease within the next 10 years.[37] This reimagined care system focuses on a timelier diagnosis, heightened access to specialty ALS clinics, and expanding the reach of people impacted by this fatal neurological disease.[37] Though August has been deemed ALS Advocacy Action Month in the U.S., these efforts can and should be conducted throughout the year to maintain the momentum of these high-impact initiatives. It has been ten years since the inaugural Ice Bucket Challenge and there is renewed engagement in this effort to celebrate its anniversary. So fill a bucket, dump it on yourself or others, and challenge friends and family to do the same. More importantly, donate to this amazing cause to find a cure and make ALS more livable.

Conclusion

Amyotrophic lateral sclerosis is a progressive neurodegenerative disease, and though considered rare, it radically impacts both the quality and quantity of life for those diagnosed. The symptoms of ALS are severe and debilitating, decreasing the individual's and often the caregiver's quality of life. The diagnosis is one of exclusion which can extend the length of time and costs associated, between the onset of symptoms and a treatment. Though there are emerging discoveries that can lend to gene-targeted therapies in ALS, testing for such is still limited and expensive. Third-party payers control access to life-enhancing and life-prolonging treatment options and providers must find viable alternatives when recommended therapy is inevitably denied. Access to multidisciplinary care is growing but some still travel hours or days to attend an ALS-specific clinic. Research is ongoing but the 'fight to fund' continues. The outcome of an ALS diagnosis is 100% fatal and public policies should focus on three major areas to change this: finding new treatments and hopefully someday, a cure; optimizing current treatment options and access to the gold standard of care; and preventing or delaying harms associated with the disease. I hope you will join me and many others in this battle.

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