Update on ALS diagnosis and treatment

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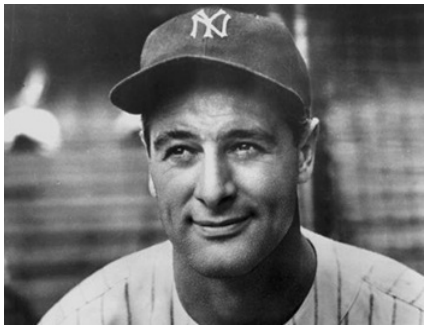
SF hospice and palliative care conference 2021

What is ALS?

- Progressive
  - Universally fatal
  - Mean survival after first symptom: **3-5 years**
- Most common adult-onset motor neuron disease
- Pathogenesis is complex and incompletely understood
- Heterogeneous
  - Clinical diagnosis of exclusion
  - No available biomarker



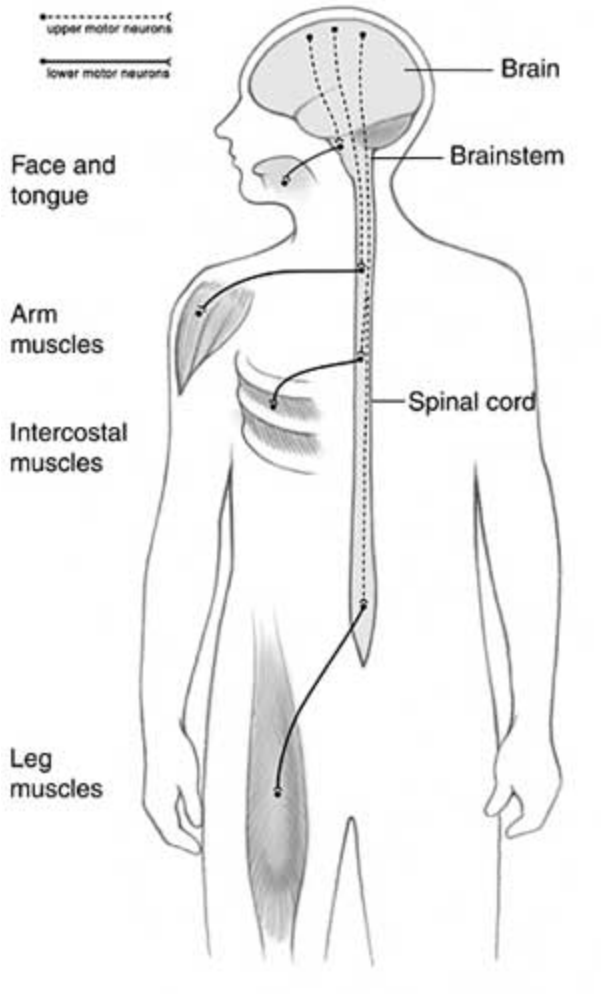
Lou Gehrig

- Poor 1938 season
- Leg> arm weakness
- Winter 38-39, many falls when skating, dropped things
- Played 2,130 games for 14 years straight
- Played 8 games 1939
- Stopped May 2, 1939
- Diagnosed June 1939
- 1940, Hoarse speech
- Died June 1941 38y/o

- 'But even from the midst of it, he saw himself "not a mere victim of a form of paralysis but a symbol of hope for thousand of suffers of the same disorder."

Kasarskis, EJ, Neurology1989;39:1243-1245

Clinical Features of ALS



- Upper motor neuron findings
  - Slow speech
  - Brisk gag and jaw jerk, brisk limb reflexes
  - Spasticity
- Lower motor neuron findings
  - Atrophy
  - Fasciculations
  - weakness

El Escorial Criteria to diagnose ALS

- UMN degeneration by clinical exam
- LMN degeneration by clinical exam or EMG
- Progressive spread of signs within a region or into other spinal or brainstem regions
- Absence of evidence of other diseases by EMG or imaging to explain the findings

ALS-Mimic Syndromes

- Radiculopathies
- Brain tumor
- Post-poliomyelitis syndrome
- Multifocal motor neuropathy
- Endocrinopathies
  - hyperparathyroidism and hyperthyroidism
- Lead intoxication
- Infections
  - Lyme disease and HIV/AIDS
- Paraneoplastic syndromes - lymphoma, MGUS

Other Motor Neuron Disorders

- Spinal Muscular Atrophy (SMN 1 gene mutations with SMN 2 and NAIP gene modifiers)
- Kennedy's disease (x-linked CAG repeat)
- Polio (post polio syndrome)
- West Nile

	Motor Neuron Disease	Neuropathy	NMJ	Myopathy
Weakness Pattern	Variable	Distal	Diffuse	Proximal
DTR	Normal or decreased	Decreased or absent	Normal or decreased	Normal or decreased
Atrophy	Yes	Yes	No	No
Fasciculations	Yes	Sometimes	No	No
Sensory symptoms/ signs	No	Yes	No	No

	Motor Neuron Disease	Neuropathy	NMJ	Myopathy
Acute Onset (Days)	Poliomyelitis Rabies	Guillain-Barre Diptheria Porphyria Poisons	Myasthenia Gravis Botulism NMJ blocking agents	Periodic paralysis Necrotic myopathies
Subacute/ chronic (weeks/years)	ALS	Many peripheral neuropathies	Myasthenia Gravis Myasthenic syndrome	Polymyositis Dermatomyositis Steroid myopathy Alcoholism Hereditary

Benefits of an earlier ALS diagnosis

- Ability to take newly approved ALS therapies
- Option to participate in clinical trials
- Access to multidisciplinary care
- Connection to ALS satellite clinics and telemedicine
- Quicker genetic testing

CONSIDER REFERRAL TO AN ALS CENTER FOR ALL CASES OF PROGRESSIVE WEAKNESS OF UNCLEAR ETIOLOGY

ALS is Heterogeneous

- The diagnosis is clinical and a process of exclusion
- Patients vary in:
  - Rate of progression
  - Regions affected during the disease course
- Accurate categorization of patients into clinical categories is of utmost importance in facilitating research into targeted therapies
- A key aspect of disease heterogeneity is cognitive-behavioral involvement including frontotemporal dementia

ALS and Frontotemporal Dementia

- Frontotemporal impairment in ALS
  - 30% FTD patients show signs of definitive or possible ALS
  - 50% of ALS patients show executive function deficits
- Common genetic cause
  - C9ORF72 gene
- Four clinical subtypes
  - ALS
  - ALS-cognitive impairment (ALSci)
  - ALS-behavioral impairment (ALSbi)
  - Frontotemporal dementia (FTD)

Why is this important? The Clinical Impact

- Reduced survival rate (Olney, 2005)
- Poor compliance (poor use of PEG, NIPPV)
- Caregiver distress
- Poor safety awareness (falls, choking)
- Inability to manage important decisions
- Implications for stem cell therapy

Related clinical issues are first ruled out

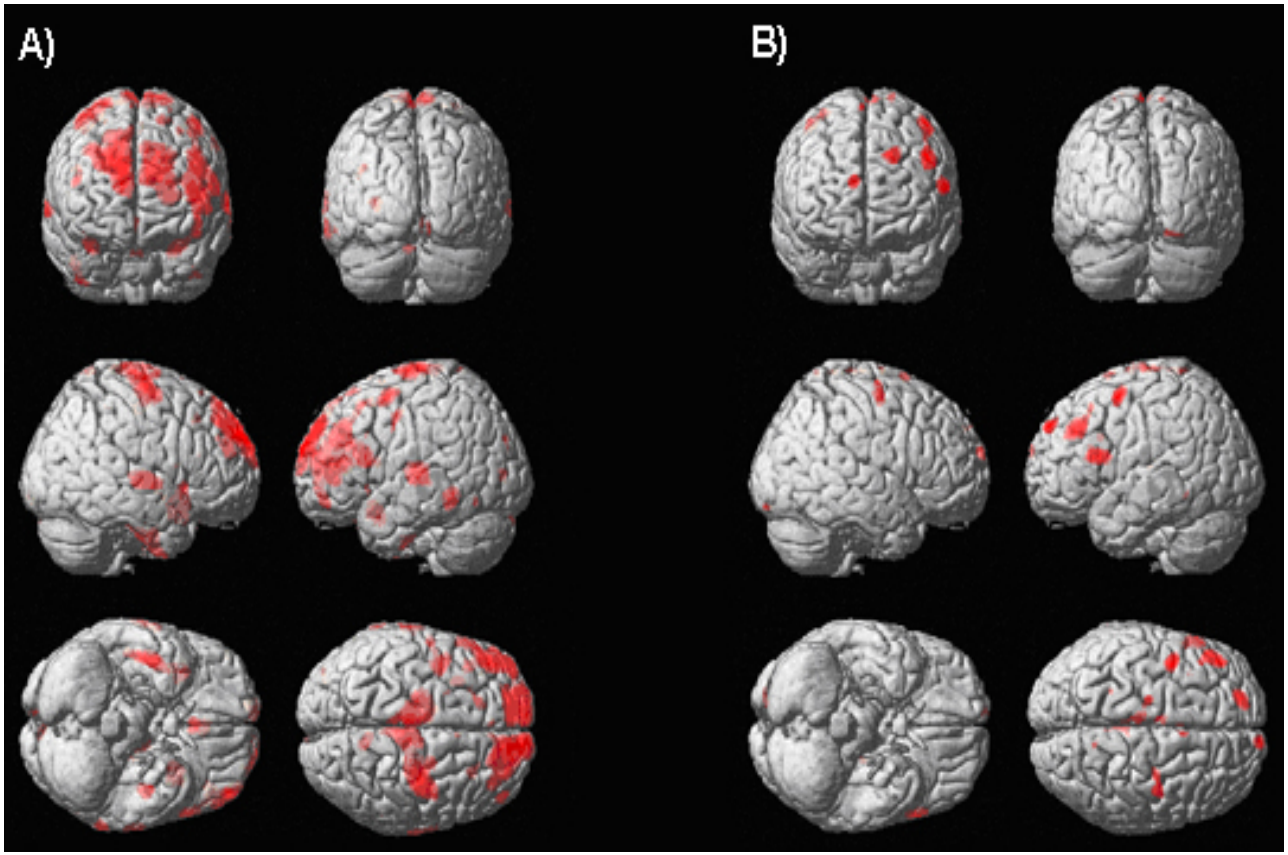
- Depression or underlying psychiatric disorder
- Pseudobulbar affect
- Forced vital capacity status (hypoxia, hypercapnia)
- Educational level/baseline intellectual functioning
- Level of disease progression which can limit testing

Major Genetic Link Identified 2011

- 10% of ALS cases are familial and 40% of bvFTD
- Families may have FTD, ALS, or both
- Mutations in TDP-43 found rarely in FTD and ALS cases
- *C9orf72* is responsible for 40% of all familial ALS cases and 25% of FTD cases
- Disease caused by expansion of a GGGGCC hexanucleotide repeat in the chromosome 9 open reading frame 72 gene
- 7% of sporadic ALS cases and 6% of sporadic FTD cases have mutations in C9orfF72

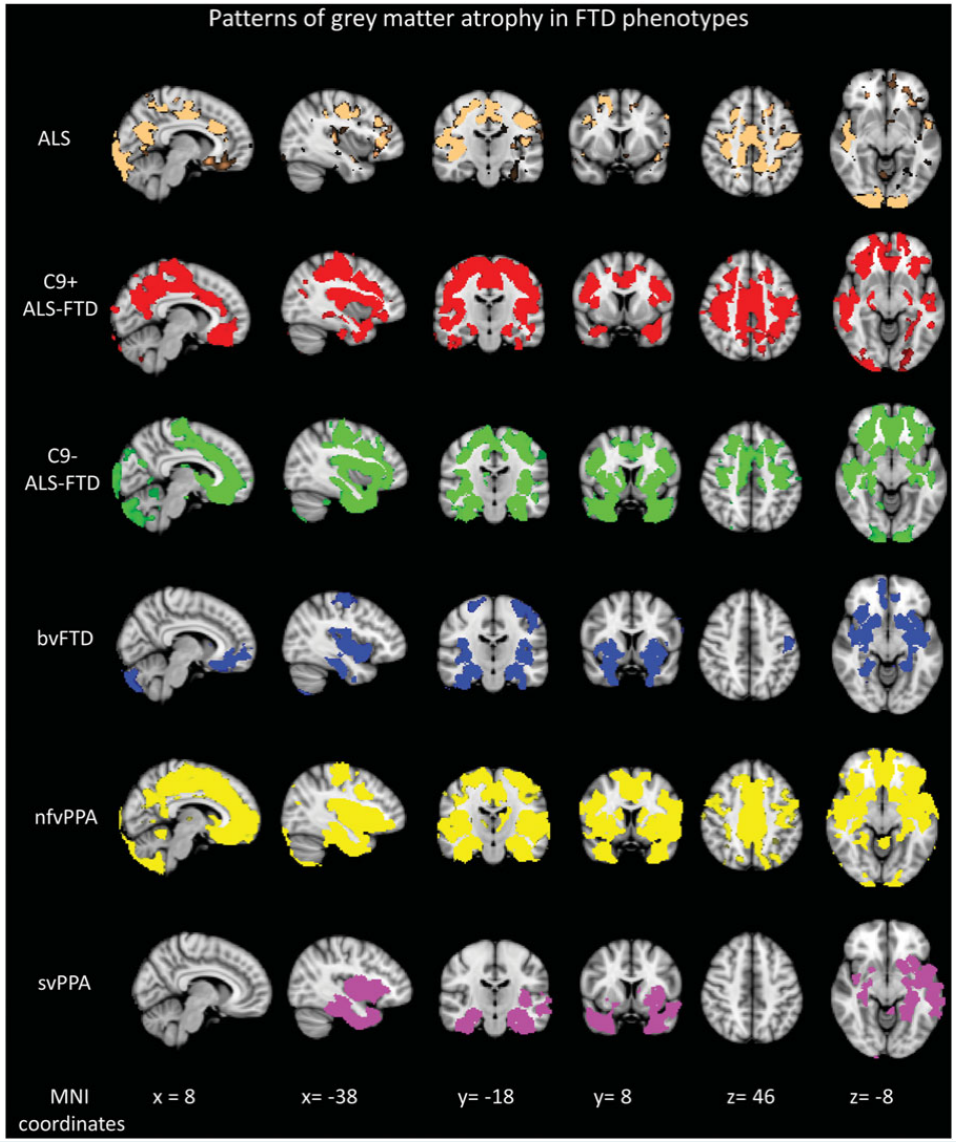
Continuum of Abnormalities

Chang et al, Neurology 2005



Patterns of gray matter atrophy

Omar et al. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 2017; 1–13



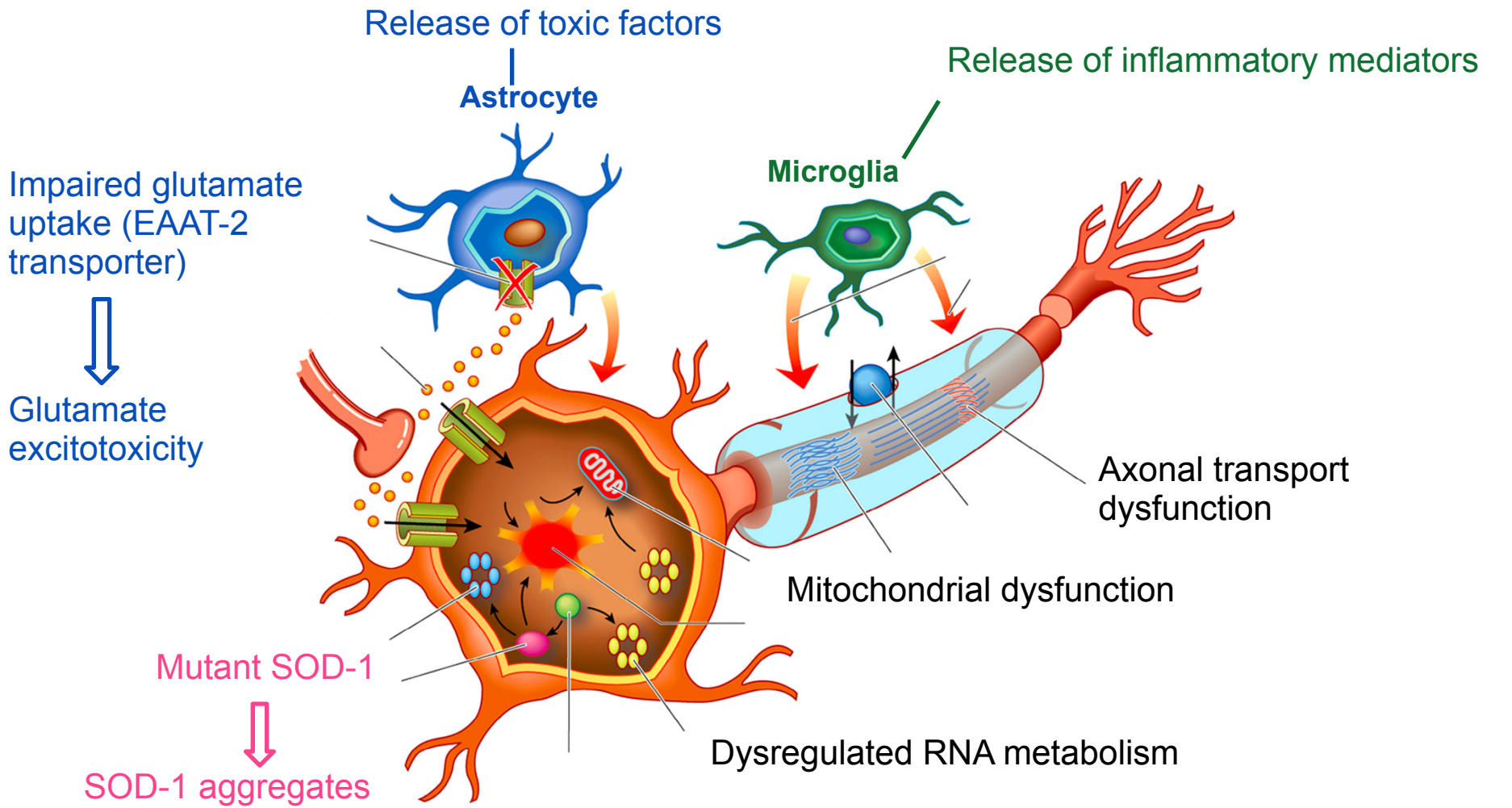
Pathology of ALS and FTD

- Inclusions in spinal cord and frontal and temporal lobes
- TDP-43 was discovered in 2006 to be the major disease protein in both ALS and the most common form of FTD. Mutations in TDP-43 cause ALS and FTD.
- The protein was recovered only from affected central nervous system regions, including hippocampus, neocortex, and spinal cord and represents the common pathologic substrate linking these neurodegenerative disorders.
- Neuronal cytoplasmic inclusions contain both TDP-43 and ubuiquitin

Environmental Risk Factors

- Chronic traumatic encephalopathy
  - For decades dementia was known to be associated with boxing
  - Trauma is associated with AD, FTD, ALS, and Parkinsonism
  - TDP43 and tau pathology found predominantly
- Increased frequency of degenerative disease in trauma causing professions
  - Soccer players at greater risk for ALS
  - NFL players 4 times more likely to get ALS
  - Military veterans 2 times more likely to get ALS
    - Higher in deployed versus non-deployed veterans

What causes ALS?



Mechanisms of Motor Neuron Degeneration

- The precise mechanisms are still unknown
- There may be convergence of multiple pathways
- There are many potential targets for drug intervention and innovative delivery methods
- Current experimental trials are targeting these pathways
- Riluzole, a glutamate antagonist, was FDA approved in 1993 to treat ALS
- Edaravone, a free radical scavenger, was FDA approved in 2017 to treat ALS

Need for safe therapies for ALS

- Riluzole was the first FDA drug approved to treat ALS
- Riluzole prolongs survival by 10% and delays disease progression modestly
- All other drugs tested to date in phase III studies either had no efficacy or caused more rapid progression compared with the placebo group, except Edaravone
- Despite the need to expedite therapies in ALS, there is a need to test the safety of drugs before larger clinical trials are initiated
- The FDA agrees that active placebo controls are critical to determine efficacy, even in stem cell clinical trials

ALS Functional Rating Scale-R

- Speech
- Salivation
- Swallowing
- Handwriting
- Cutting Food and Handling Utensils
- Dressing and Hygiene
- Turning in bed and adjusting clothes
- Walking
- Climbing Stairs
- Dyspnea
- Orthopnea
- Respiratory Insufficiency

Stem cells and ALS

- Healthy supporting cells can extend survival of mutant motor neurons
- Neural stem cells transplanted into mice extends survival
- Stem cells have been safely injected into the spinal cord of ALS patients
- More work is needed to keep cells alive and make sure they stay in the right place

Brainstorm update

- Stem cells are removed from the bone marrow of patients with ALS and modified to secrete neurotrophic factors
- Cells are put back into the muscle or spinal fluid with no adverse events
- Phase 2 trial results suggested there may be small reductions in the rate of disease progression
- Phase 3 trial results just in and the treatment was not approved by the FDA due to benefit only in a small portion of rapidly progressive ALS patients

First platform trial for ALS starting now

- ALS has the largest drug pipeline of any neuromuscular disease
- Over 130 companies currently focusing on ALS
- Need to accelerate trials for patients with ALS

Healey Center for ALS

"I lost the privilege of working on the human time clock on January 6, 2018 – the ALS clock is a lot faster" Sandy – Person with ALS

Right to try and expanded access

- Need pharma approval to provide the drug
- FDA and IRB approval (accelerated for ALS<2 weeks)
- Need funding
- Provides a way to provide people not eligible for clinical trials to obtain drug

Caution about certain alternative therapies for ALS

- Expensive stem cell options in the US and other countries
- Excessive supplement use
- Detoxification programs
- Unusual diets
- Taking clinical trial medications off label

http://alsuntangled.com/

Steps in the Management of ALS patients

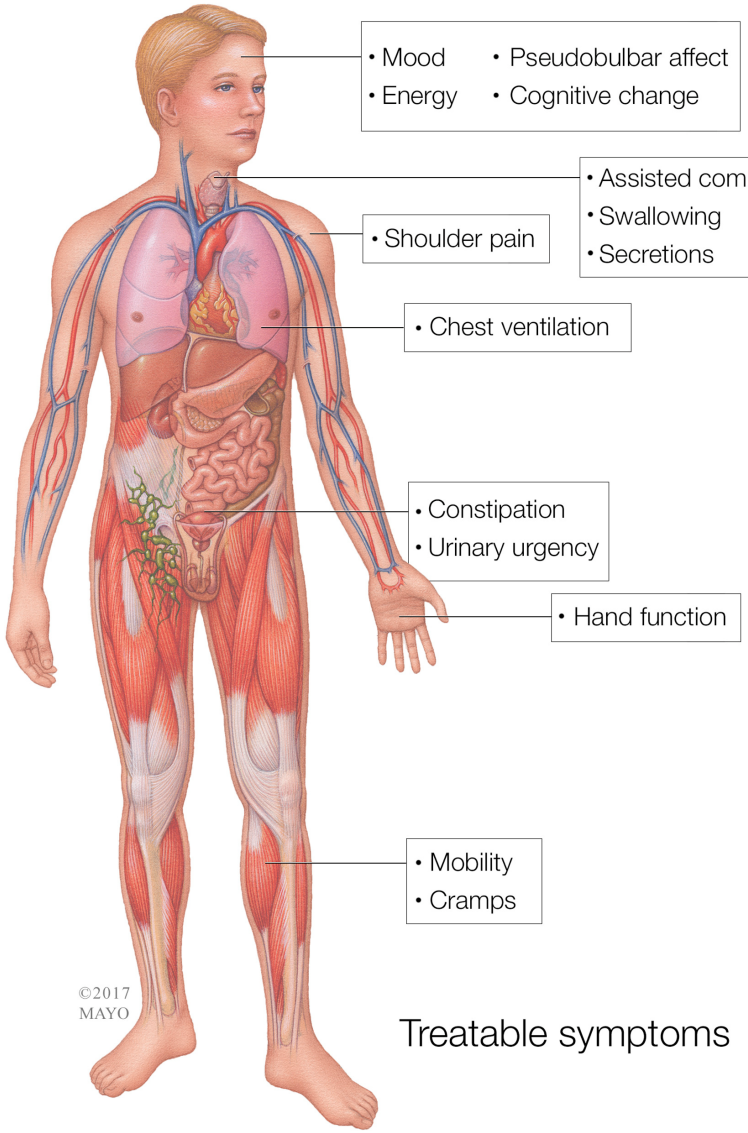
- Making the diagnosis and breaking the news
- Starting treatments that slow the disease process
- Managing respiratory insufficiency
- Managing dysphagia / preventing malnutrition
- Treating symptoms that reduce quality of life
  - Sialorrhea, pseudobulbar affect, spasticity, cramps
  - Maintaining mobility
  - Multidisciplinary care
  - Palliative care

AAN Practice Guidelines Neurology 1999;52:1311; 2009; 73: 1227-1239

Changes in management of adults for better quality/ quantity of life

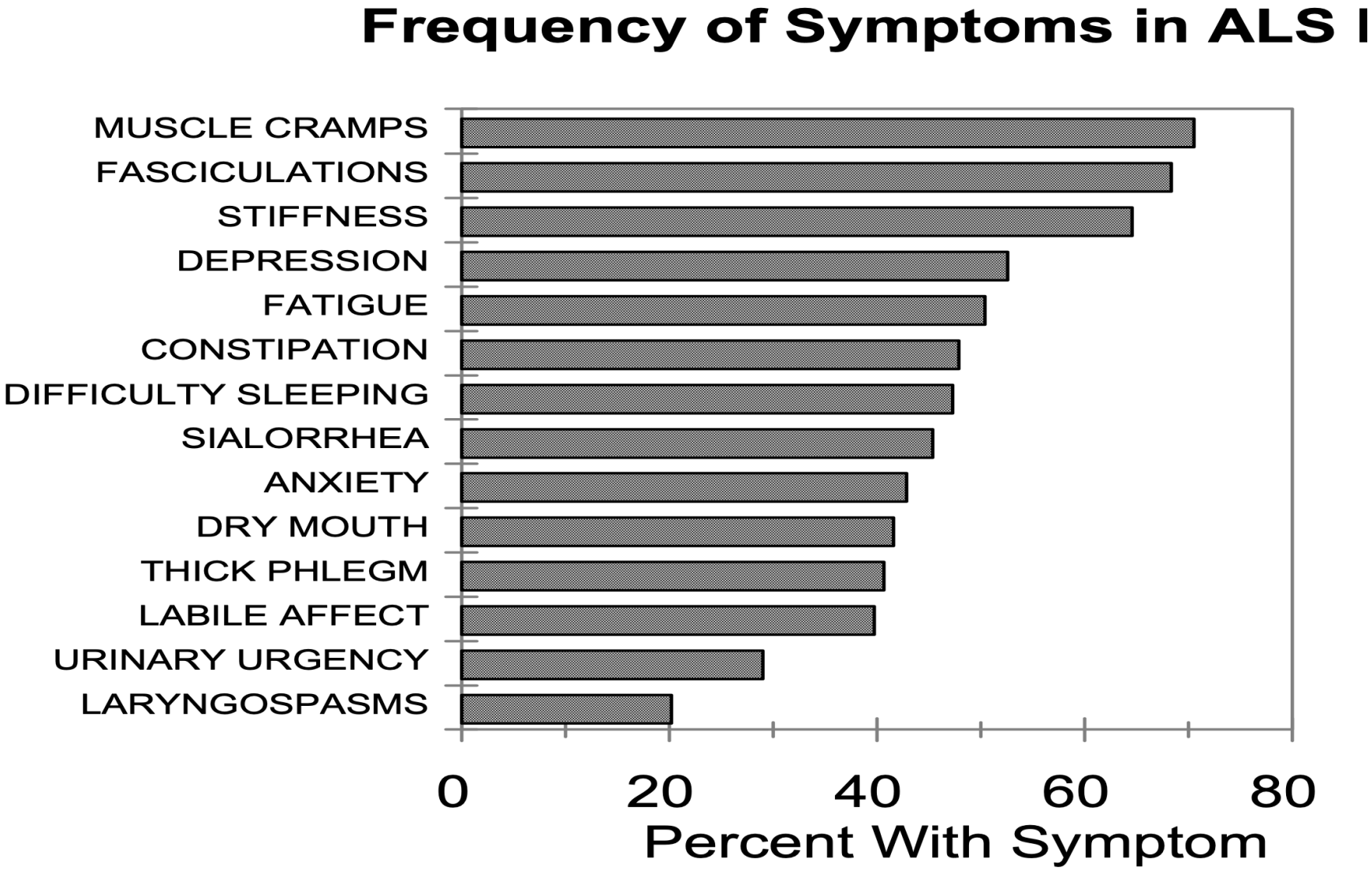
- More adult ALS centers available for multidisciplinary care
- Improved diagnostic process with genetic testing and pre-natal testing options
- More clinical research opportunities for adults
- Better recognition of symptomatic issues
- Examples of definitive changes in practice
  - Nutrition
  - Respiratory Care
  - Depression
  - Mobility
  - Multidisciplinary care

Treatable symptoms in ALS



Treatable symptoms

Mayo Clin Proc. 2018 Nov;93(11):1617-1628.



Forshew and Bromberg, 2003

Hard questions patients often ask

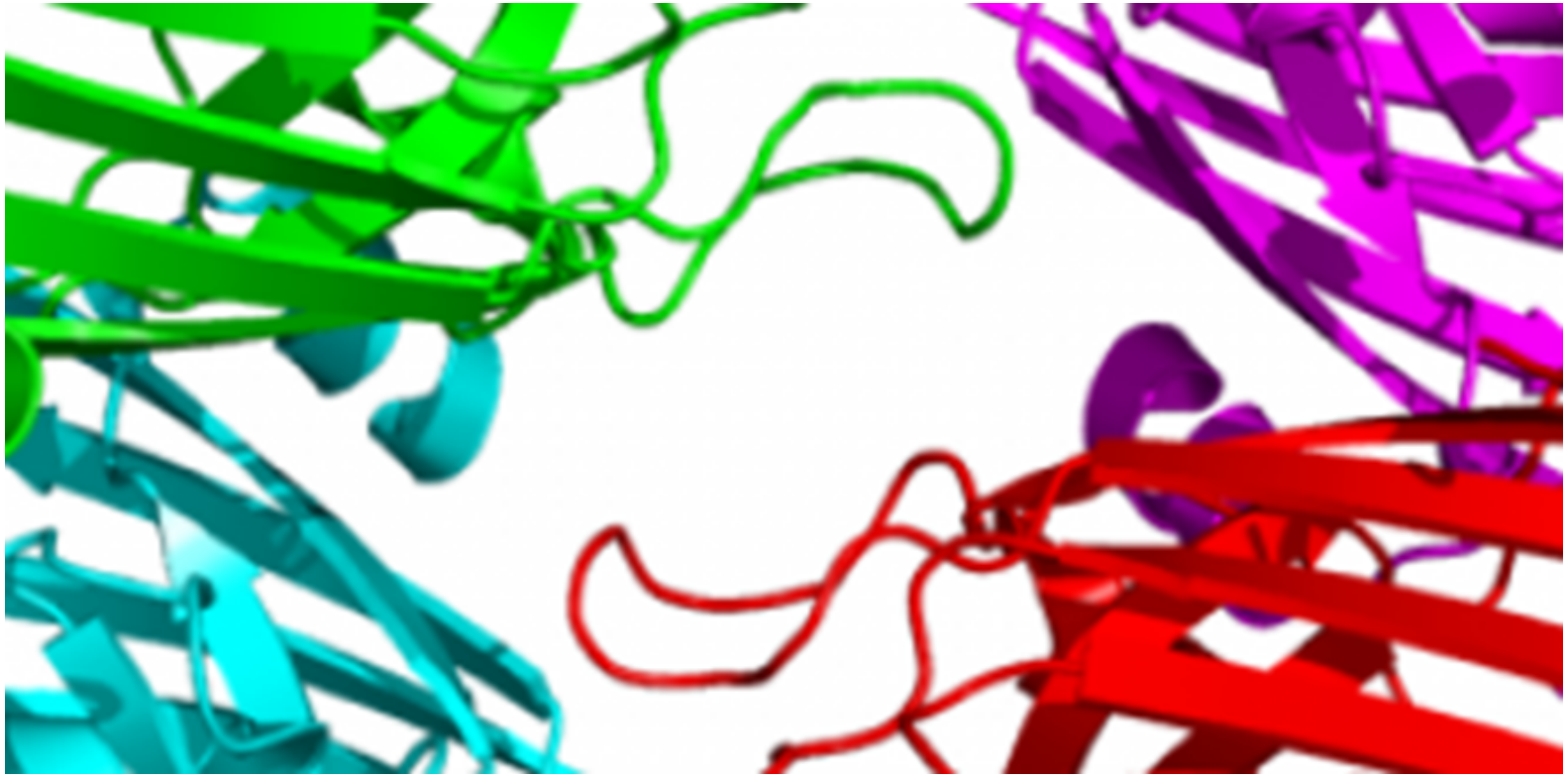
- Should I get genetic testing?
- I am losing weight, should I get a feeding tube?
- I am short of breath now, what are my options?
- I am falling and my family is also worried I am not safe to drive
- Should I exercise?
- People don't understand me when I speak and writing is hard for me
- I don't go out of the house because of fear of accidents
- How do I know if I am depressed?

Should I get genetic testing?

- Would it change management of the condition knowing the genetic cause? (new treatments available or clinical trials)
- Has anyone in the family with similar symptoms already been tested?
- Is there a current clinical trial for the suspected diagnosis where testing may be free?
- Is the patient considering having children and if so is pre-natal testing available?
- Does the patient's insurance or non-profit organization cover doing the testing for the suspected diagnosis?
- Has the patient undergone genetic counseling first?

Free genetic testing and counseling

ALS GAP provides clinical genetics services to pALS who are under the care of a registered NEALS clinician
https://www.neals.org/als-trials/news/als-gap-update



Designer DNA therapy for ALS

- Antisense oligonucleotide therapies for familial ALS
- Viral therapies such as designed for SMA
- Gene therapy studies targeting sporadic ALS

Curr Opin Neurol. 2018 Oct;31(5):648-654.

I don’t go out of the house because of fear of accidents

- Anticholinergics
- Condom catheters
- Suprapubic catheters
- Male and Female Urinals
- Develop a good bowl regimen

I hate having constipation

- Increase fluids
- Increase fiber
- Prune juice
- Consider stool softeners and other OTC aids
- Consider lactulose

What can I do about cramps?

- Massage, hot baths, stretching
- “Hot Shot” drink
- Tegretol and Baclofen
- Mexiletine
- Quinine Sulfate
  - Prescribe qualaquin if patients have prescription coverage
  - Order quinine sulfate from Canada if no prescription coverage
  - Drink tonic water which contains low doses of quinine

Spasticity is hard to treat

- Balance between too stiff and too loose
- Use baclofen, diazapam, dantrolene, mementine, and tizanidine
- Consider a baclofen pump
- Botox for focal spasticity

Pseudobulbar affect

- Hard to diagnose
- Traditionally managed with amitriptyline
- SSRIs have a mild effect on symptoms
- New drug dextromethorphan hydrobromide and quinidine sulfate (nuedexta)

CNS-Lability Scale

Applies never	Applies rarely	Applies occasionally	Applies frequently	Applies most of the time
1	2	3	4	5

1. There are times when I feel fine one minute, and then I'll become tearful the next over something small or for no reason at all.

2. Others have told me that I seem to become amused very easily or that I seem to become amused about things that really aren't funny.

3. I find myself crying very easily.

4. I find that even when I try to control my laughter, I am often unable to do so.

5. There are times when I won't be thinking of anything happy or funny at all, but then I'll suddenly be overcome by funny or happy thoughts.

6. I find that even when I try to control my crying, I am often unable to do so.

7. I find that I am easily overcome by laughter.

How do I know if I am depressed?

- Exclude a respiratory problem
- Exclude pseudobulbar affect
- Improve nutrition
- Make sure sleep is good
- Consider referral to a counselor
- Start antidepressants as needed

Sleep

- Most sleep problems are mechanical for ALS patients
  - Lack of appropriate breathing support at night
  - Difficulty positioning during the night for comfort
- Start treatment with herbal or mild over the counter aids
- Consider sedating antidepressants
- Lastly, try the benzodiazepines

Palliative Care for ALS

- Talk about end of life issues throughout the disease process
- Enroll in hospice as soon as eligible
- Utilize home care if not hospice eligible
- Transitions programs becoming more common
- Continue to follow in an ALS multidisciplinary clinic while in hospice
- End-of-life act option

Multidisciplinary ALS Team

Core Members

- Neurologist
- Nurse
- Speech pathologist
- Dietitian
- Respiratory therapist
- Physical therapist
- Occupational therapist
- Social worker
- Rehabilitation technologist
- Psychologist
- Genetics counselor

Consultants

- Rehabilitation physician
- Pulmonologist
- Gastroenterologist
- Cardiologist

Associates

- Research scientists
- ALSA and MDA

SUMMARY

- Advances in genetics are leading to more precise diagnoses and potential disease therapies
- Nutrition and breathing problems can be better treated now
- Medications are available to treat many of the symptoms of patients
- Equipment advances enable patients to be more independent than ever
- Communication options are continuing to expand
- Independence is possible even with advanced disease states including use of the end-of-life option act

Acknowledgements

The UCSF ALS Multidisciplinary Team:

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Madelon Thomson (Social Worker)

David Besio (Nutritionist)

Christoph Karch (Fellow)

Jennifer Coggiola (Speech therapist)

Carrie Grouse (Fellow)

Not pictured: **Mira Kleytman** (Respiratory therapist)

Mercedes Paredes (Physician)

Colleen Meier (Respiratory therapist)

Deborah Ha (Speech therapist)

Virginia Santos (Clinic Coordinator)

Miriam Crennan (Occupational therapist)

SFBA HPNA
SAN FRANCISCO BAY AREA CHAPTER
Hospice & Palliative Nurses Association

Break!

We'll be back in 15 minutes

Visit sfbahpna.org to learn more about us!

San Francisco Bay Area Chapter
Hospice & Palliative Nurses Association

UCSF Health

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ALS Association
Golden West Chapter

Madelon Thomson, LCSW
License Clinical Social Worker

ALS ASSOCIATION
Golden West Chapter

GWC Regions

Central Coast: Monterey, San Benito, San Luis Obispo, Santa Clara and Santa Cruz

Central Valley: Inyo, Kern, Madera, Merced, Fresno, Tulare, Kings, Mariposa and Stanislaus

North Bay: Alameda, Contra Costa, Del Norte, Humboldt, Lake, Marin, Mendocino, Napa, San Francisco, San Mateo, Solano and Sonoma

South: Los Angeles, Santa Barbara and Ventura

South East: San Bernardino and Riverside

Hawaii: Hawaii, Oahu, Maui, Kauai, Molokai, Lanai

ALS ASSOCIATION
Golden West Chapter

Golden West Chapter Programs and Services

- 1840 families served in 2020
- 1:1 care management – a care manager assigned to each family who registers with the Chapter
- Referrals to nearly 30 multidisciplinary clinics in the Chapter's territory
- More than 30 support groups offered virtually each month (see next slide)
- DME and AAC equipment loan programs throughout the Chapter
- Quality of Life grants for respite care, equipment repair/purchase, emergency assistance, kids' enrichment activities
- Educational webinars on topics such as ALS research, dysphagia, palliative care, estate planning, mindfulness, caring for the caregiver, and more

ALS ASSOCIATION
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Support Groups

Support groups are crucial learning forums focused on reducing isolation and promoting strategies for meeting the challenges of living with ALS. The Golden West Chapter provides more than 30 monthly support groups throughout our service area that feature both educational speakers and small group discussions. **All groups are currently held via Zoom.

Sample Support Group Topics and Presentations Include:

- Nutrition and ALS
- Self-Care Tools and Tactics
- Breathing/Respiratory Equipment Commonly Used in ALS
- In Home Skilled Nursing Care
- Assistive Communication Technology
- Estate Planning/5 Wishes
- Adaptive Yoga

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Regional Support Groups

- Bakersfield/Kern County
- East Bay
- Fresno
- Glendale
- Hawaii – all islands
- Central Coast
- Loma Linda/Murrieta
- Long Beach/Carson
- Napa
- North Bay/Santa Rosa
- Palm Springs
- Palo Alto
- Pomona
- San Fernando
- San Francisco
- San Jose
- San Luis Obispo
- Santa Barbara
- Solano County
- Turlock
- Ventura County

Population Focused Groups

- Bereavement
- Familial ALS
- LGBTQ
- Loved Ones
- Mindfulness
- Spanish
- Trach/Vent
- Veterans
- Families Raising Young Children

Caregiver Support Groups - Regional

- North Bay Caregiver
- LA Caregiver
- Santa Rosa Caregiver
- Ventura Caregiver
- East Bay Caregiver
- San Jose Caregiver

ALS ASSOCIATION
Golden West Chapter

Physical Therapy Management in ALS

Monika Patel, PT, DPT
Board Certified Neurologic Clinical Specialist
Assistant Clinical Professor at UCSF/SFSU DPT Program

Early stage

- Independent with mobility, function, ADLs, minimal to no activity limitations and participation restrictions
- **+ Muscle weakness in certain muscle groups**

Middle stage

- Increased number of impairments (weakness, stiffness, pain), activity limitations, inability to participate in daily tasks/social participation
- **Need for compensatory interventions and assistance from others**

Late stage

- **Total dependence for function and mobility**
- Severe weakness of the limb, trunk, and neck muscles

Dal Bello-Haas, 2002

Symptoms of ALS where PT has an impact

- **Muscle weakness/atrophy:**
  - Baseline muscle testing
  - Recommendations ⇢ rest, exercise, stretching program, use of supportive devices, functional mobility training

- **Muscle stiffness and cramps:**
  - Testing for spasticity and range of motion
  - Recommendations ⇢ daily stretching program, hydration, heat, exercise, avoid over-use

Bello-Haas, Kloos, Mitsumoto et al., 1998

- **Fatigue:**
  - Recommendations ⇢ energy conservation, taking rest breaks, taking naps, getting good sleep, improve breath support, use of assistive devices

- **Pain:**
  - Recommendations ⇢ Stretching program to weaker muscle groups, assistive devices to reduce pressure (low back), neck supports (collar), pressure relieving devices, positioning, heat, massage.

Bello-Haas, Kloos, Mitsumoto et al., 1998

Bello-Haas, 2018

Patients often ask us in clinic ….

Is it Safe to Exercise?

Can it help to slow the disease?

What type of exercise do you recommend?

Exercise Recommendations

Exercise DO's	Exercise DON'TS
✓ DO resistance training for unaffected/ minimal weak muscles AND Stretching Exercises daily – active and passive if needed	✗ Don't exercise to the point of fatigue or overwork muscles
✓ DO light aerobic exercise in the form of walking, stationary bike/cycling, swimming.	✗ Don't push yourself until you are sore the next day
✓ DO take short rest breaks and save energy so you can continue doing self care activities	✗ Don't strengthen weak muscles

Assistive/Adaptive Devices

- **Early Stage:** PALS may benefit from a cane or hiking poles.
- **Middle Stage:** PALS may need a more support device such as a walker and an AFO or ankle support if there is foot drop
- **Late Stage:** PALS will likely need a manual wheelchair or power wheelchair for primary mobility

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Imbalance/Falls

- Imbalance may result from progressive muscle weakness (quads, foot drop),spasticity, fatigue that will affect activities such as walking, transfers, and ADLs.

- **Recommendations:**
  - PT referral (home or outpatient) for balance exercises
  - Use an assistive device and/or bracing
  - Raise up surfaces for transfers
  - Use gait belt for transfers
  - Caregiver and Family Training for assistance
  - Use of Hoyer lift for transfer
  - Remove potential tripping hazards
  - Bathroom modifications – grab bars, shower chair
  - Understand limits of walking – transition to wheelchair

Majmudar et al. 2014

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Occupational Therapy and Management of ALS

Jessica Mok, MA , OTR/L

OT Role in Managing Patients with ALS

Maintain independence ADLs, IADLs, Work, Leisure and to improve quality of life

- Prescribe appropriate assistive device and durable medical equipment
- Activity adaptation to promote safety, independence and conserve energy
- Home modification
- Caregiver training

Arbresman, M; and Shreard, K ,2014
Lewis M. and Rushman S., 2007

The Early Stage of ALS

Symptoms:

- Hand weakness (intrinsic muscles, thumb)
- Affect fine motor skills such as buttoning, zipping, difficulty opening Ziploc; pulling out a parking ticket
- Cramping

Recommendations:

- Activity Adaptation
- Energy conservation
- Home modification
- Splints
- ROM

Del Bello- Haas, V.;Kloss, A; Misumota, H, 1998

The Disability Stage of ALS

Symptoms:

- Significant weakness in arms
- Increased difficulty with transfers
- Increased fatigue
- Difficulty accessing phone or computer
- Neck weakness

Recommendations:

- Activity adaptation
- Caregiver training (AAROM, Transfer training, ADLs)
- Home modification
- Energy conservation
- Splinting & bracing
- DME (Power wheelchair)

Del Bello- Haas, V.;Kloss, A; Misumota, H, 1998

The Late Stage of ALS

Symptoms:

- Nearly fully dependent with ADLs and transfers
- Wheelchair bound
- Very minimal movement at all extremities , trunk , head weakness
- May not be able to drive the power wheelchair

Recommendations:

- Caregiver training (PROM, transfer training)
- Positioning and pressure relief
- Edema management
- Wheelchair modification
- Contractures management
- DME (hospital bed, hoyer lift)

Del Bello- Haas, V.;Kloss, A; Misumota, H, 1998

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Energy Conservation

Why?

- Muscle weakness causing fatigue

How?

- Pacing; Prioritize your activities
- Activity modification; incorporate rest breaks

Outcome?

- Improve quality of life

Lewis M. and Rushman S., 2007

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Speech-Language Pathology & ALS

Patricia Liu, M.A. CCC-SLP

Speech-Language Pathology & ALS

Communication

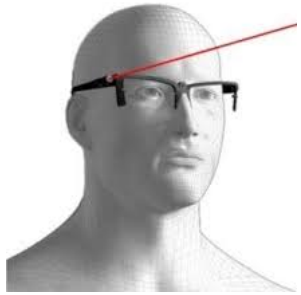
Speech-Language Pathology & ALS

Communication

High-Tech

Mid-Tech

Low / No-tech



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Speech-Language Pathology & ALS

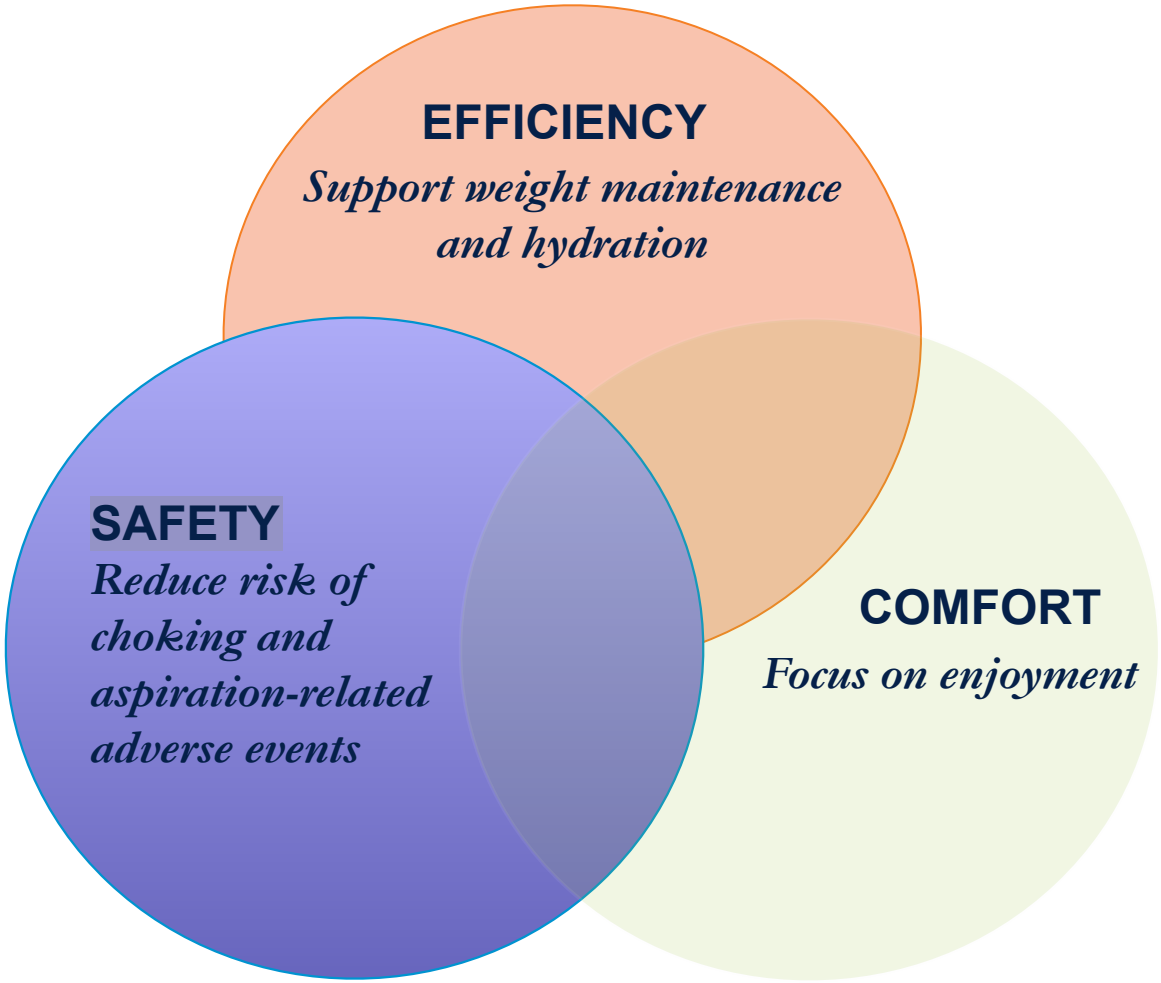
Communication

Consider:

- Multi-modal communication
- Slowing pace of conversations
- Allowing time to prepare longer messages
- Establishing reliable yes / no / maybe gestures
- Routines, environmental management, consistency to anticipate needs

Speech-Language Pathology and ALS

Dysphagia Management



Speech-Language Pathology & ALS

Dysphagia Management

- ***Assessment***
- **Patient report of symptoms**
- **Dietary intake**
- **Pulmonary function & cough**
- **Bulbar function**
- **Clinical Exam**
- **Instrumental Assessment?**

Intervention

Texture modification

Solids

Regular, soft- and bite-sized, minced/moist, purees

Liquids

Thin, slightly, mild, moderately thick

Carbonated

Strategies and Maneuvers

Liquid wash, extra swallows

Portion control

Bolus administration (spoon / cup / straw)

Bolus hold, chin tuck, supraglottic swallow

Mindful eating and drinking

Energy conservation

Pausing intake w/ dyspnea

Resting on NIV prior to meals

Speech-Language Pathology & ALS
Dysphagia Management

- Oral care interventions have been shown to reduce the incidence of pneumonia in elderly populations.

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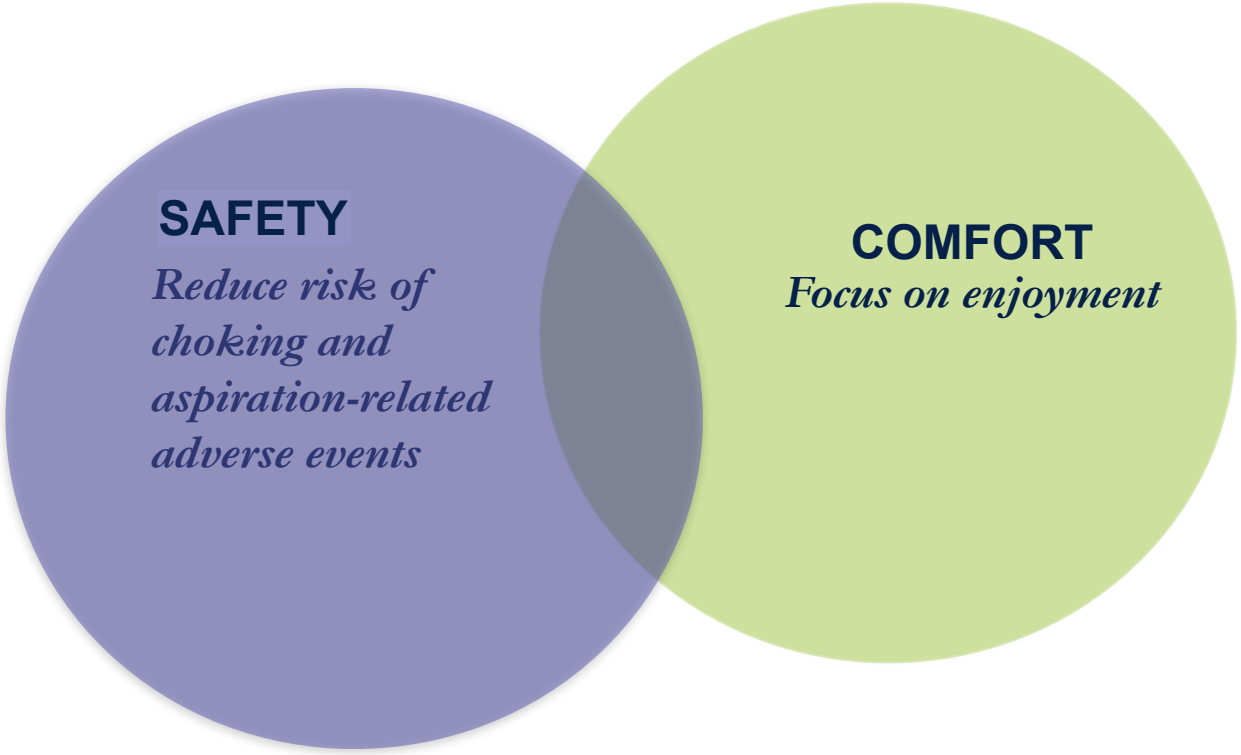
Speech-Language Pathology and ALS

Dysphagia Management

After recommendation for feeding tube placement



Speech-Language Pathology and ALS

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Nutrition for ALS

David Besio, MS, RD
Senior Outpatient Dietitian

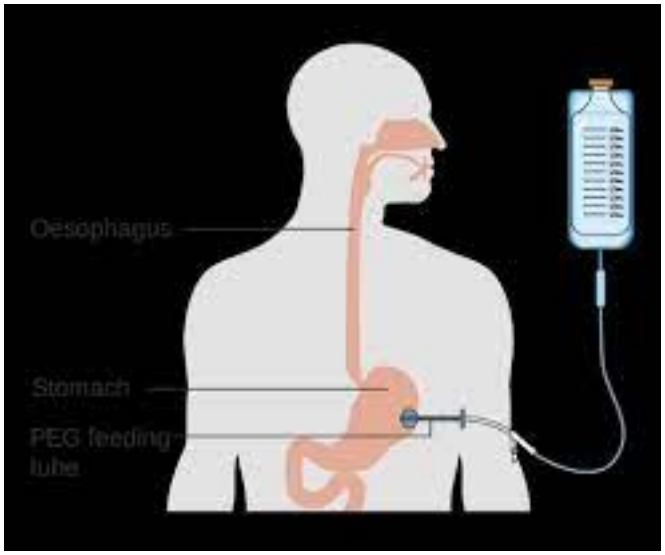
Adequacy of Nutrition Intake for Weight Maintenance

- Potential symptoms which prevent adequate intake
  - chewing/swallowing trouble
  - arm/hand weakness
  - shortness of breath/fatigue
  - increased energy expenditure
  - psycho-social barriers
  - poor appetite
  - GI problems
  - TF intolerance

Paganoni et al, Muscle and Nerve, 2011
Korner et al, BMC Neurology, 2013
Kasarkis et al, Am J Clin Nutr, 2014

Adaptive Responses

- Solutions to promote adequate intake
  - Food/fluid consistency modifications
  - eating aids
  - breathing support
  - high calorie high protein diet
  - feeding tube
  - social/emotional support and guidance
  - GI symptom management



Genton et al, Clinical Nutrition, 2011
Wills et al, Lancet, 2014

Managing GI problems

- Diet modifications
- Fluid intake
- Tube feeding complications/complaints
- Medication management
- Vitamin supplementation management

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Respiratory Therapy and Management of ALS

Mira Kleytman, RCP, RRT

ALS Patients Entering Home Hospice

- Have FVC <30% predicted
- Life expectancy of < 6 months
- Rapidly progressing ALS
- Need additional resources at home
- Underinsured and need equipment at home

Common Respiratory Equipment

1. Respironics Trilogy Non-invasive vent, can be used invasively
2. BiLevel (aka BIPAP)
3. Res-Med non-invasive vent, can be used invasively (Astral NIV)

Hayek Medical BiPhasic Ventilation

- Negative Pressure Ventilation with use of Chest Schell
- Available for home use for patients who are not tolerating positive pressure ventilation via BiPap or NIV

Amara view mask ventilation

Sip and puff ventilation

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Nasal Mask and Chin Strap

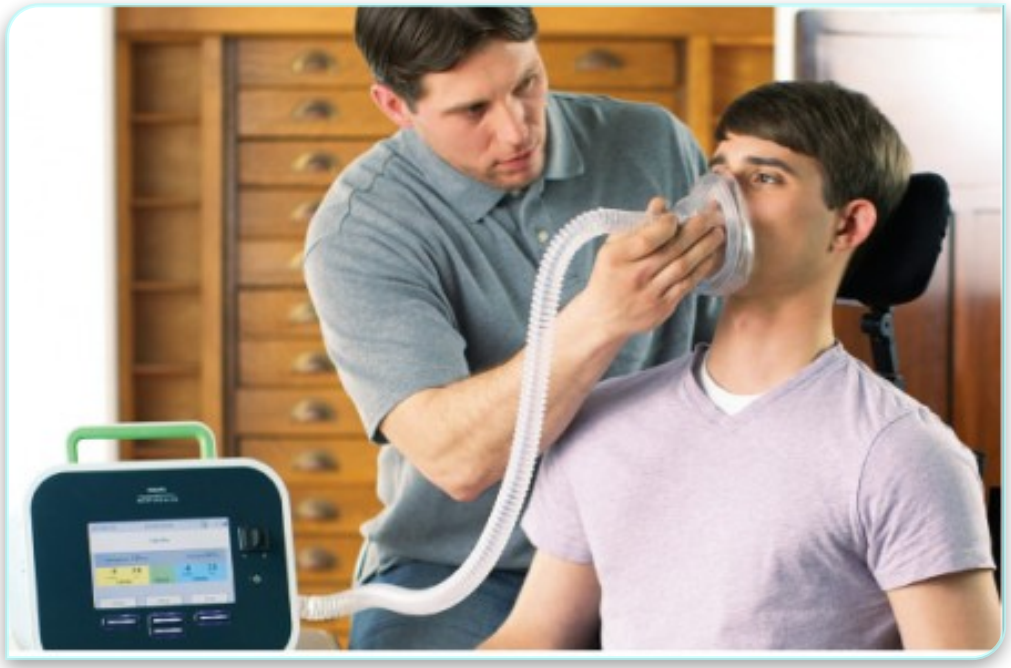
- Chin strap is used to help keep mouth in closed position when patient is on NVI and avoid unintentional leak.

Full Face Mask & Total Mask

- Used when patient is unable to keep mouth closed
- Used when unable to keep mouth closed, to relive pressure points on bridge of nose

Respironics T-70 Cough Assist

- Used for secretion clearance
- Provides Positive Pressure for Lung Expansion
- Provides expiratory pressure to mimic cough
- Can be used for breath stacking exercise
- Can be used non-invasively by mask or invasively via tracheostomy tube



Therapy Vest

- Not used frequently in ALS
- Provides secretion clearance therapy via oscillation vibration to chest wall
- Used for Cystic Fibrosis, COPD and Bronchiectasis
- Does not help bring secretions up in ALS

Devilbiss Suction Aspirator with rechargeable Battery 7305P-D

- Should be portable
- Patient may need to take with them when outside of home

Oxygen

- Not ordered for ALS prior to Hospice
- Is known to suppress respiratory drive and cause C02 retention
- Can be given safely together with NIV or BiPap as Bleed in.

Oxygen connected to Trilogy NIV

Oxygen tubing connected to Oxygen Inlet Adapter with the Philips Respironics Trilogy Ventilator *Sold Separately*

Terminal Extubation

- Considered with quality of life is no longer meaningful
- Acute irreversible illness
- Communication is no longer possible via eye gaze device
- Patient runs out of financial means to support care at home
- Requires administration of opioids and benzos with down titration of vent support.
- Possible in home setting or ICU
- Organ donation possible if done in ICU


THANK YOU
FOR ALL YOU DO

UCSF Health

Case Study

Mark Terrelonge, MD, MPH
Professor, Neurology

Patient History

TG is a 56 right handed women who came to UCSF for evaluation of motor neuron disease.

- **October 2019 – February 2020**
  - Weakness in her right hand and burning in her shoulder.
  - Progressive issues with dexterity in her right hand over the next 4 months.
  - EMG in February 2020 with upper and lower motor neuron changes concerning for motor neuron disease.

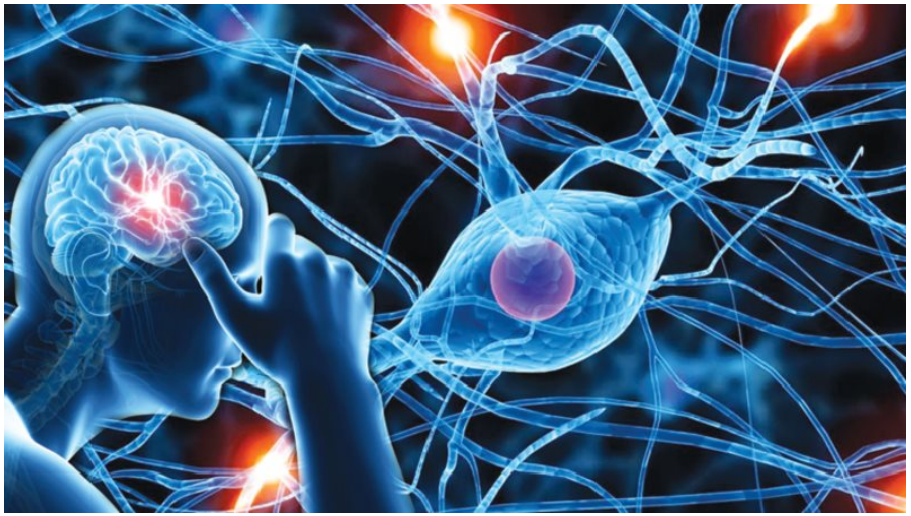
Patient History *cont…*

- **Other symptoms**
  - Slurred speech
  - Choking episodes
  - Excess saliva in the left side of her mouth
  - 3-5 pound weight loss in past 4 months
  - No breathing difficulties
  - No sleep difficulties

February 2020 - Neurologic Exam

Mental Status

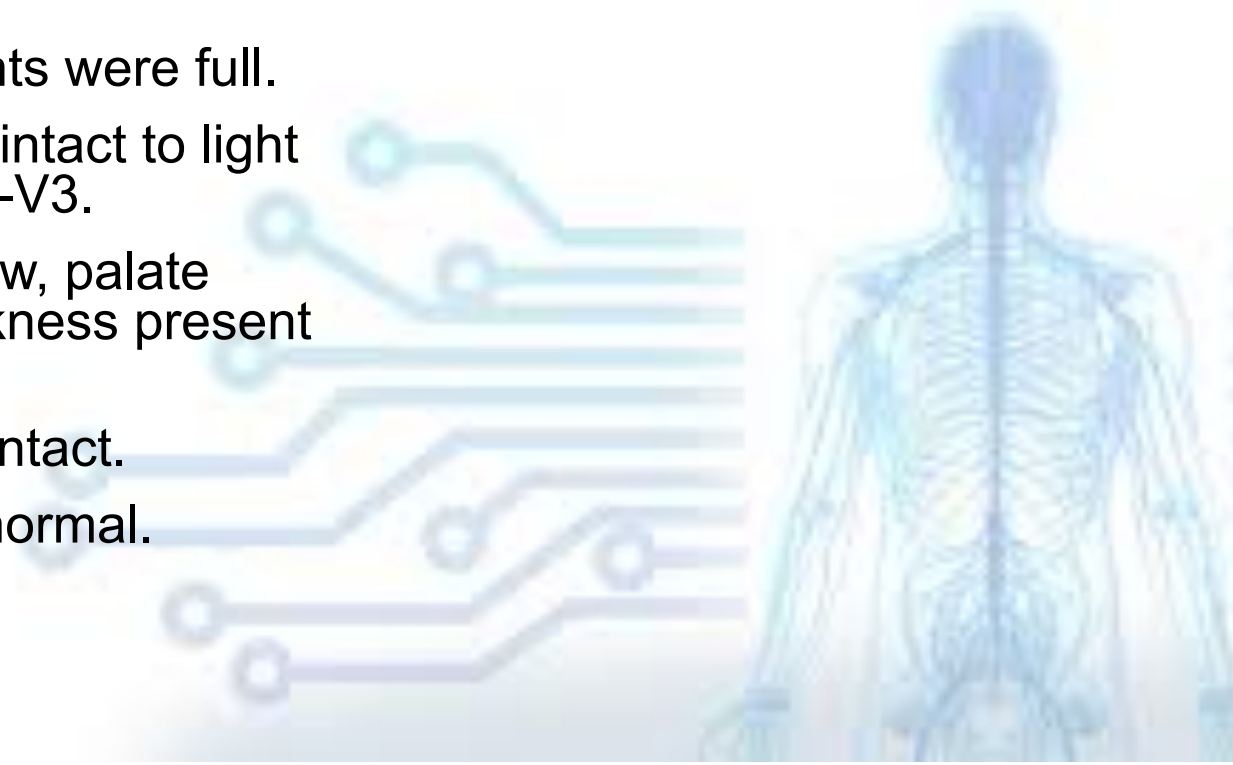
- Patient is alert, attentive, and oriented to recent events.
- Speech was coherent and fluent without dysarthria or aphasia.
- Memory, comprehension and ability to follow commands were intact.



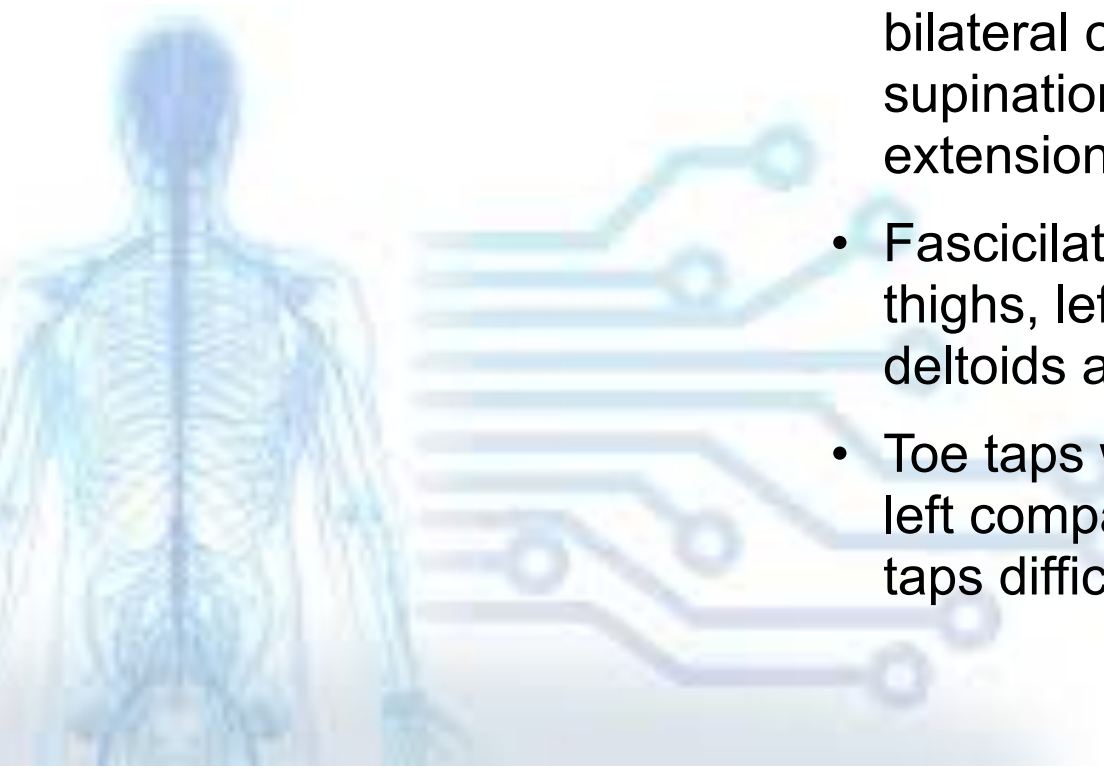
Neurologic Exam *cont…*

Cranial Nerves

- Pupils were round and reactive to light.
- Visual fields were full to confrontation.
- Extraocular movements were full.
- Facial sensation was intact to light touch bilaterally in V1-V3.
- There was no face, jaw, palate atrophy. Tongue weakness present bilaterally.
- Hearing was grossly intact.
- Shoulder shrug was normal.
- Jaw jerk with clonus.



Neurologic Exam *cont…*

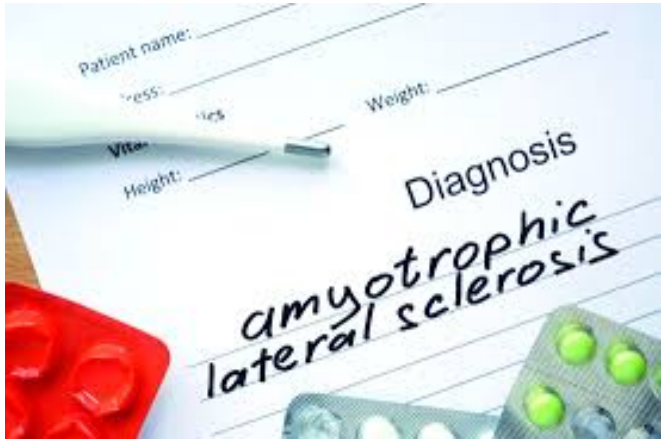


Motor Exam

- Revealed decreased muscle bulk throughout most notable thought the hands and spastic catch on bilateral on arms (pronation/ supination) and legs (knew extension/flexon).
- Fascicilations present in bilateral thighs, left lateral calf, bilateral deltoids and forearms.
- Toe taps were slightly slow on the left compared to the right (finder taps difficult due to weakness).

Additional Data

- FVC 2.36L (67%), PEF 305 LPM (77%), MIP -56 (-58 supine), MEP +80
- EMG/NCS (Feb 4, 2020): Interpretation:
- 1. Motor neuropathy with diffuse acute denervation in all muscles tested - including bilateral upper and lower extremities, as well as bilateral trapezii (fibs noted in bilateral trapezius, APB, FDI, and TA; and right deltoid and biceps. Large units with decreased recruitment in bilateral trapezius and TA; and right deltoid and biceps)
- ALS-FRS: 39/48



First Visit Plan

- Mimic Labs: CPK, LFTs, TSH, free T4, SPEP, IFE, and lyme antibody titer
- Start Riluzole 50mg BID; serial LFTs
- Consider Radicava
- Consider TUDCA 500mg to 2 grams daily

March 2020

- Worsening dysarthria
- Increased saliva
- Interesting in clinical trials
- Delayed Radicava due to insurance
- Asked for referral to Palliative Care Symptom Management

• Multidisciplinary Team •
Madelon Thomson, LCSW
Patricia Liu, M.A., CCC-SLP

May 2020

- Started Radicava, in addition to Riluzole and TUDCA

June 2020

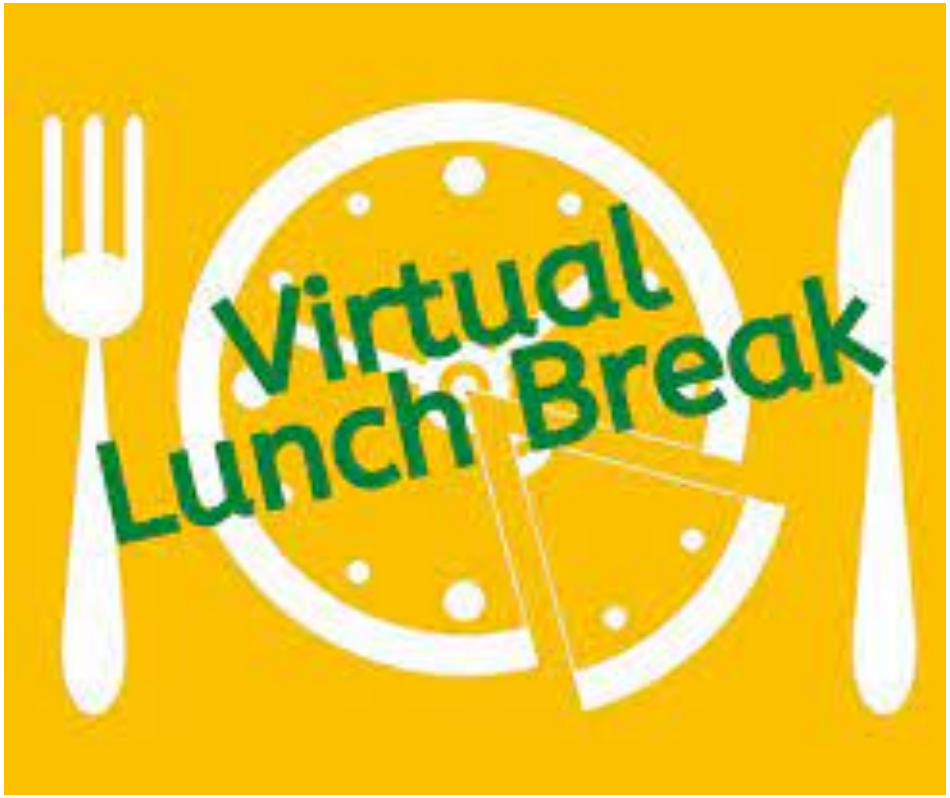
- Worsened swallowing
- Admitted for PEG tube placement in late June 2020
  - IR unable to place PEG tube due to anatomy
  - GI could not approach endoscopically
  - Unable to do surgery due to poor bedside PFTs
  - NGT placed instead

• Multidisciplinary Team •
David Besio, MS, RD
Senior Clinical Dietitian
Eve Cohen, BSN, RN

July 2020

- Decided against PEG tube placement and transitioned to Hospice

Questions?


Virtual
Lunch Break

Palliative Care for ALS: It Takes a Village

Kara Bischoff, MD
Medical Director
UCSF Outpatient Palliative Care Service
May 2021

The UCSF Outpatient Palliative Care Service

- Launched in 10/2017
- Transdisciplinary team: RN, SW, chaplain, MDs, practice coordinator
- Longitudinal co-management
- Telehealth
- Close collaboration with the ALS team:
  - Co-location
  - Shadowing
  - Sharing many patients
  - Frequent communication
  - Educational sessions / case conferences

Patients with ALS

- On average, very receptive to palliative care
- High palliative care needs

  … in patients and family caregivers
- Incredibly satisfying patients to care for

The Role of Palliative Care,
in addition to the wonderfully robust ALS team

1. Symptom management
   - Physical and psychological
2. Advance care planning
   - Illness understanding
   - Values and priorities
   - Help making specific decisions: e.g. DPOA, FT, trach, location of care, hospice, EOLOA
3. Psychosocial and spiritual/existential support to patients and family members

A Case: Mr. JL

- 65yo M living in Crescent City, river kayaker, outdoors man, husband, 23yo SIL with autism + epilepsy
- Progressive weakness since 6/2016 → functional decline, fatigue, dysphagia with weight loss → dx ALS 10/2017
- Respiratory weakness a/w SOB

Symptom Management in ALS: It takes a Team

- Weakness and functional decline
- Dysarthria
- Sialorrhea (drooling) and feeding difficulties
- Weight loss
- Respiratory decline
- Insomnia
- Pain
- Depressed and anxious mood
- Pseudobulbar affect

Symptom Management in ALS: It takes a Team

A person with ALS may experience new loss every week or every month

By focusing on quality of life, treatment of symptoms, and support of the caregivers, much can be offered

Functional Loss: We can help

- Maximizing physical support and mobility
  - Neck support
  - Walkers
  - Wheelchairs
  - Transfer devices e.g. hoyer lift, glide mat
  - Stair glide
- Maximizing safety and skin integrity
  - Hospital bed and special mattresses
  - Splints
  - Shower chair or tub bench
  - Grab bars

Functional Loss: Dysarthria
Communication Devices

- Helping families develop and evolve communication strategies
- Voice amplifiers
- Voice recorder and computer software for voice banking
- Specialized computers and software
  - Speech generating
  - Switches or touch screen for alternative access
  - Eye gaze systems

Symptoms: Sialorrhea

- 50% of patients with ALS experience this
- Due to poor handling of saliva rather than increased production
- Mechanical: Suction, cough assist
- Pharmacologic approaches
  - Anticholinergics e.g. glycopyrrolate 1-2mg tid, scopolamine, caution in the frail and elderly
- Interventional approaches
  - Salivary gland botulinum toxin injections

Symptoms: Weight Loss

- Good nutrition associated with increased survival and higher quality of life in ALS
- Feeding tubes reduce burden on patient and family when meals take >1 hour
- Evidence-based guideline recommends considering PEG if weight loss and dysphagia and if respiratory capacity >50% of normal*
- When patients want a PEG we try to prepare them
- When patients don't want a PEG we try to understand why

Respiratory Weakness and Dyspnea

- First presents as shortness of breath when lying down and during exertion
- Important to monitor respiratory function throughout the disease
  - FVC is what we focus on most
  - Gives information about prognosis and helps guides decisions about bipap, PEG, tracheostomy, and hospice

Dyspnea – Non-invasive Ventilation (bipap)

- Associated with improved quality of life
- Alleviates symptoms of dyspnea and improves sleep, energy, alertness
- May increase survival by up to 18 months
- Caution if severe bulbar dysfunction

Bourke SC et al. Lancet Neurol. 2006

Dyspnea

- Mindfulness strategies
- Opiates – low doses usually work, e.g. start concentrated morphine soln 5mg SL q2H prn
- Benzodiazepines – if opiates fail or anxiety is a major component

Symptoms: Insomnia

- Important to identify underlying causes
- Night-time hypoxia and hypercarbia common
- Anxiety, claustrophobia
- Other causes – difficulty moving in bed, pain, leg cramps, fasciculations
- Treatments:
  - Trazodone
  - Mirtazapine
  - Other

Pain

- Multiple causes
  - Leg cramps, spasticity
  - Immobility
- Non-pharmacologic treatments
  - Range of motion exercises, repositioning, heat, therapeutic mattresses, relaxation, distraction
- Pharmacologic treatments
  - Treat spasticity with baclofen, cyclobenzaprine
  - Follow WHO guidelines, including use of opioids

Symptoms: Neuropsychiatric

- Depression and anxiety common
  - Mirtazapine, SSRIs and tricyclics
  - Support groups and counseling
- Pseudobulbar affect – sudden uncontrollable outbursts of laughter or tearfulness (20-50% pts)
  - Not a mood disorder
  - Treatments: dextromethorphan/quinidine (Nuedexta)

ALS and Frontotemporal Dementia

- Cognitive impairment (executive function) in 35-51% of pts – data from 3 studies
  - Most are minor
- Approximately 15% pts meet criteria for frontotemporal dementia
  - Impaired judgment, attention, and planning/ organizing; apathy, personality changes; short-term memory often spared
  - Often difficult to diagnose due to communication impairments
- Family caregiver support is often needed!

ALS: Burdens and Suffering

- Survey of n=100 patients with ALS, living in Oregon and Washington (97% lived at home, 24% had hospice services)
  - 65% said they were a burden on their family
  - 48% reported financial hardship due to ALS
  - 56% reported they would consider physician-assisted suicide

Ganzini L et al. NEJM, 1998

Resources for Patients and Caregivers

- ALS Association
  - Support groups
  - Respite services
  - “Loan closets” for equipment
- Medicare
- Hospice
  - Recommend early referral, but encourage expensive equipment (communication equipment, power wheelchairs) prior to referral

A Case: Mr. JL

- 65yo M living in Crescent City, river kayaker, outdoors man, husband, 23yo SIL with autism + epilepsy
- Progressive weakness since 6/2016 → functional decline, fatigue, dysphagia with weight loss → dx ALS 10/2017
- Respiratory weakness a/w SOB
  - Bipap initiated 12/2017
  - Benefitted from mindfulness and opioids for SOB
- Weakness, change in roles, support for wife
- Goals & values: “I don’t want to ride the elevator to the bottom floor.”
- Concerned about burdening his wife

Advance Care Planning and ALS

- An ongoing process from Day 1
- Focus on:
  - Illness understanding
  - Goals and values, including cultural and religious
  - Fears
  - Identify surrogate decision-maker
  - Feeding tubes
  - Endotracheal long-term mechanical ventilation
  - Hospice

Long-Term Invasive Mechanical Ventilation (LTMV)

- Prevalence varies by country
  - 27% in Japan
  - U.S. per 1993 study showed range of 1% - 14%*
    - Decision related to individual medical center practices and physician attitudes toward its use
    - Mean yearly cost $153,252
- Often unplanned, due to emergent intubation

*Moss et al. Neurology 1993

Who Chooses LTMV?

- Cohort study of n=72 patients with ALS (all hospice-eligible) at academic medical center
- The 14 (19%) who chose tracheostomy
  - Younger
  - More likely to have young children
  - Higher household incomes
  - Reported higher levels of optimism about their disease, including belief in imminent cure
- After 36 months on LTMV, half retained optimism and enjoyment in life

Rabkin JG. Amyotroph Lateral Scler, 2006

Choosing LTMV

- Advantages:
  - Prolongs life
  - Less aspiration pneumonia
  - Some patients continue to engage in meaningful activities, even when only eye movement remains
- Disadvantages:
  - Disease continues to progress → paralysis
  - Frequent suctioning can cause distress, sleep disruption
  - Caregiver/family burden
  - Out-of-pocket costs

Discussing LTMV

- Begin discussions well in advance of crisis
- Address all the relevant concerns, including time-specific goals, caregiving plan, and financial costs
- For those who choose LTMV, discuss conditions of withdrawal

Medicare Hospice Criteria

- At least one of following
  - Critically impaired breathing (FEV1<30% predicted)
  - Rapid progression
  - Critical nutritional impairment including insufficient intake, weight loss, dehydration
  - ≥1 life-threatening complication
- Medicare criteria can fail to identify many hospice-appropriate patients*

  If you think of hospice, it's probably time

* McCluskey et al. J Pall Med, 2004

Hospice and ALS

- Early hospice referral provides critical home care services, symptom management, and caregiver support
- Hospice patients more likely to:
  - Die in preferred location
  - Die outside of the hospital
  - Receive morphine

Ganzini et al. Neurology 2002

End of Life Options Act

- Patients with ALS think of PAD relatively commonly
- Concern about being able to self-administer meds at the time that prognosis <6 mo
- Does need 2 MDs to weigh in +/- mental health specialist, 15-day waiting period

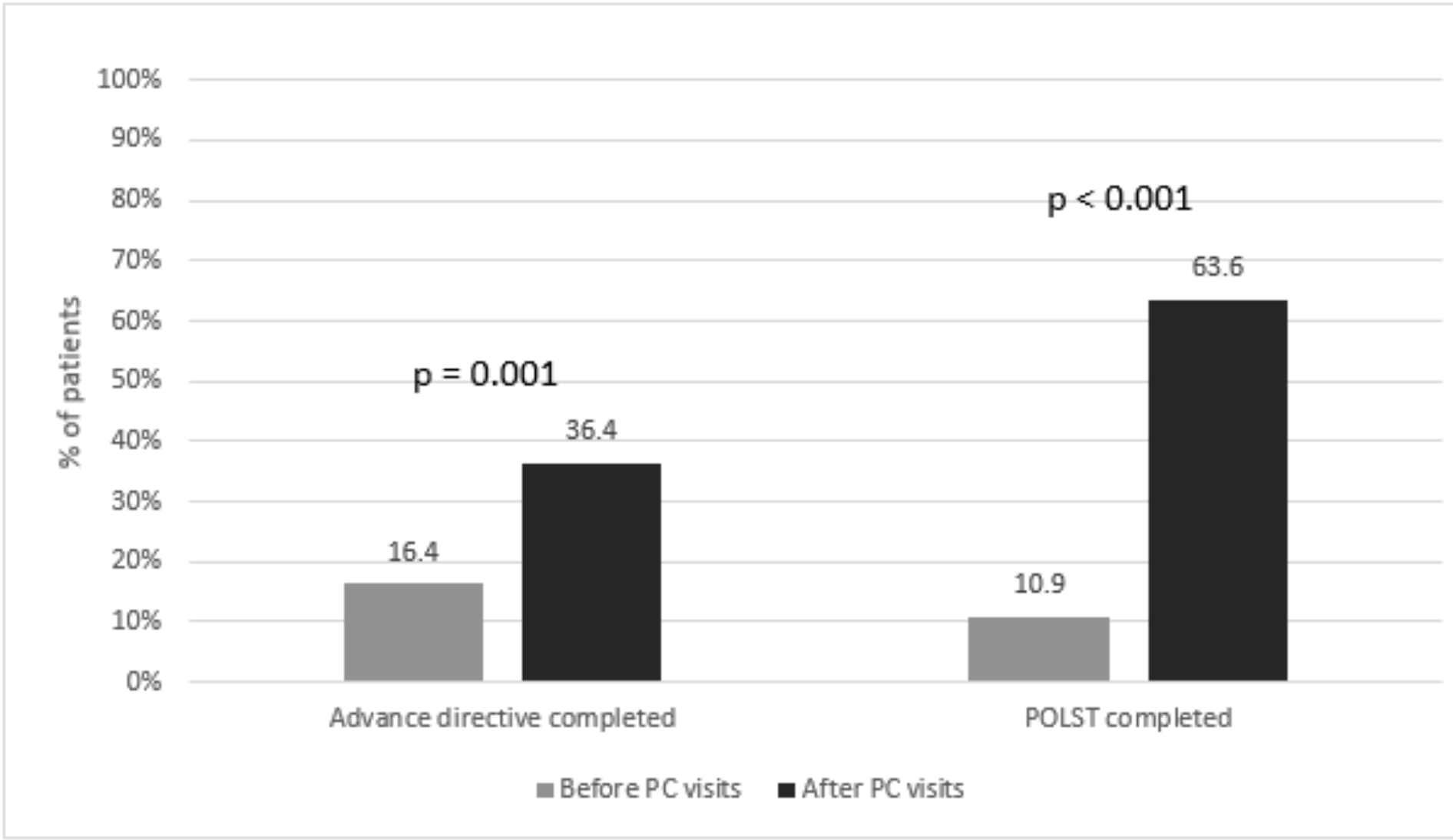
OUR EXPERIENCE

Table 2. Palliative Care Needs Identified and Interventions*

Area of need	Need identified	Intervention provide
	% (n)	*% (n)*
Pain	49.1 (27)	43.6 (24)
Non-pain symptoms	98.2 (54)	94.5 (52)
Psychosocial needs	81.2 (45)	78.2 (43)
Spiritual needs	40.0 (22)	29.1 (16)
Advance care planning/Goals of care	98.2 (54)	96.4 (53)
Family caregiver support	Not measured	96.4 (53)

* Needs could be identified by palliative care clinicians at any point in the course of care. I
interventions could be provided by palliative care clinicians at any point in the course of ca

Figure 2: Trends in Advance Care Planning with Palliative Care



PC: Palliative care

POLST: Physician Orders for Life-Sustaining Treatment

Table 3: End-of-life Care for Patients Who Died

End-of-Life Care	**n=29**
	% (n)
Used hospice	75.9 (22)*
Hospice length-of-stay	*n*
3-7 days	1
8-30 days	4
>30 days	17
Location of death	*% (n)*
Home	75.9 (22)
Hospital	17.2 (5)
Other care facility	6.8 (2)
Prescribed MAID medication	40.7 (11)
Took MAID medication	29.6 (8)
	Mean (median, range)
Time between initial PC visit and death (months)	7.67 (7, 1 19)

* 19 of 22 patients who used hospice died at home

Palliative Care for ALS: Take-Home Points

- There's a lot that can be done through collaborative, transdisciplinary care:
  - Physical & psychological symptom management
  - Advance care planning
  - Support for family caregivers

Thank you!

SFBA HPNA
SAN FRANCISCO BAY AREA CHAPTER
Hospice & Palliative Nurses Association

Break!

We'll be back in 5 minutes

Visit sfbahpna.org to learn more about us!

San Francisco Bay Area Chapter
Hospice & Palliative Nurses Association

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Case Studies / Break-Out Rooms

Eve Cohen, RN
Palliative Care Nurse

Case Study #1 "JL"

64 y/o male diagnosed with ALS in May 2020. Six months ago (Nov 2020), patient was working and independent with ADLs. A PEG was placed last month and is tolerating tube feeds though experiencing increased constipation. Recently, he experienced a rapid progression of his ALS – mostly chair-bound and now on BiPAP 24/7. Patient lives with his wife who is his primary caregiver though she is still trying to work from home.

Palliative Care has been meeting with patient and it has become apparent that patient remains unsure of his goals of care and has not completed a POLST. His wife is requesting hospice.

Case Study #1 "JL"*cont…*

On hospice admission - Patient c/o:

- Shortness of breath, anxiety and constipation.

- Allergies: NKDA

- **Medications:**
- Riluzole 50 mg BID
- Morphine 5 mg Q4 hours PRN dyspnea (concentration 20mg/ml)
- Senna 2 tabs BID

- **Group Discussion:**
- *What are the issues?*
- *What other information would be helpful to know?*
- *What pharmacological intervention might you recommend?*
- *What non-pharmacological intervention might you recommend?*

Case Study #2 “PT”

63 y/o female with bulbar ALS. Patient cannot speak and communicates through typing on her iPad. She had a PEG tube placed 6 months ago though continues to have ongoing issues of constipation and diarrhea. Patient has been struggling with mucous and coughing which is very bothersome and burdensome. The “coughing fits” result in patient getting upset and anxious. She lives with her husband and her daughter visits often and helps care for her.

During hospice admission visit, patient is very emotional and is crying through most of the visit. The hospice team has learned that patient has EOLOA medications.

She has worked with the Palliative Care clinic to qualify for EOLOA and is now struggling to figure out when she wants to take these medications.

Case Study #2 "PT" *cont…*

Allergies: Morphine

Medications:

- Lasix 20 mg PEG Qdaily
- Celexa 30 mg PEG Qdaily (concentration 10mg/5 ml)
- Nuedexta 1 capsule PEG BID
- Glycopyrrolate 1-2 mg PEG TID
- Mucinex 600 mg PEG QID
- Tylenol 640 mg PEG Q6 hours (concentration 160 mg/5 ml)
- Dilaudid 2 mg PEG Q4 hours PRN pain (concentration 1mg/1ml)
- Senna 10 ml PEG BID PRN constipation (concentration 8.8 mg/5ml)

Group Discussion:

- *What are the issues?*
- *What other information would be helpful to know?*
- *What pharmacological intervention might you recommend?*
- *What non-pharmacological intervention might you recommend?*

Thank you for attending!

UCSF Health

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Hospice & Palliative Nurses Association