ALS and Other Motor Neuron Diseases: An Introduction

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Disclosures

- I have the following relevant financial relationship(s) in the products or services described, reviewed, evaluated or compared in this presentation.
  - University of Louisville School of Medicine
    - Employee
- I have no relevant nonfinancial relationship(s) to disclose.

Educational Grant

Exhibitors/Sponsors

Objectives

- Review the history and clinical course of ALS and other motor neuron diseases
- Discuss the diagnostic workup and efforts to find anything instead of ALS
- Discuss standard of care and the multidisciplinary ALS clinic
- Discuss the need to continue the care outside of our clinic, in the community

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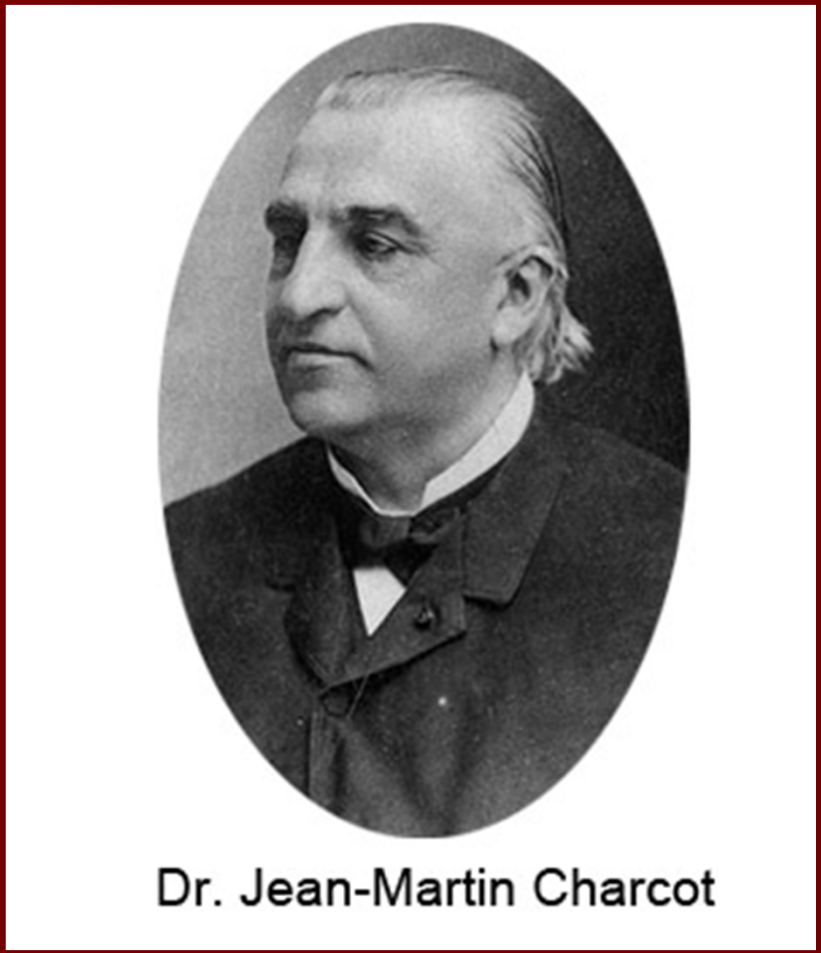
History and clinical course

- A historical perspective (with an embedded review of neuroanatomy)
  - Primary lateral sclerosis
  - Spinal muscular atrophy
  - Sclérose latérale amyotrophique
- Clinical course

Paris, 1860s

“Anatomo-Clinical Method”

- Document clinical signs during life
- Record anatomical findings at death
- Correlate clinical findings to autopsy findings



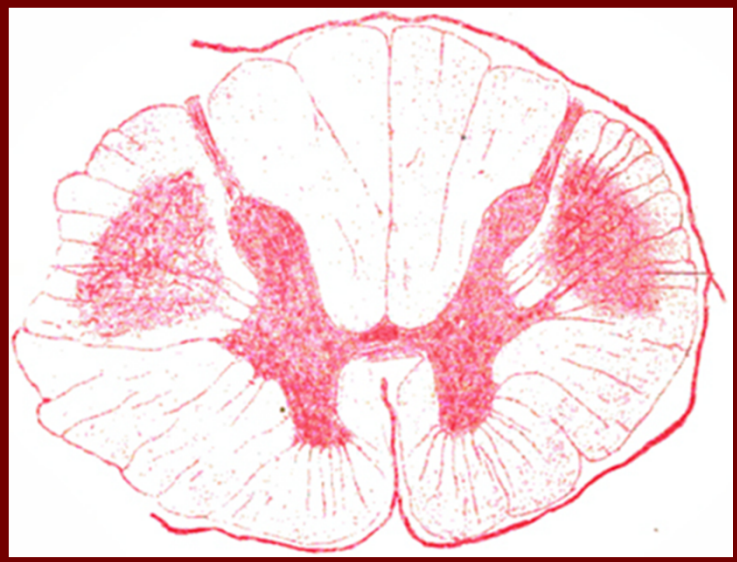
Dr. Jean-Martin Charcot

Primary Lateral Sclerosis

- Clinical signs during life:
  - Slowly progressive weakness & spasticity, “contractures”
  - No sensory disturbance
  - No cognitive disturbance
  - No involuntary movements
  - No bowel/bladder incontinence
  - No muscle atrophy

Primary Lateral Sclerosis

- Anatomical findings at death:
  - Sclerosis (scarring) of the lateral columns "white matter" throughout the length of the spinal cord
  - Gray matter (including anterior horn cells) unaffected



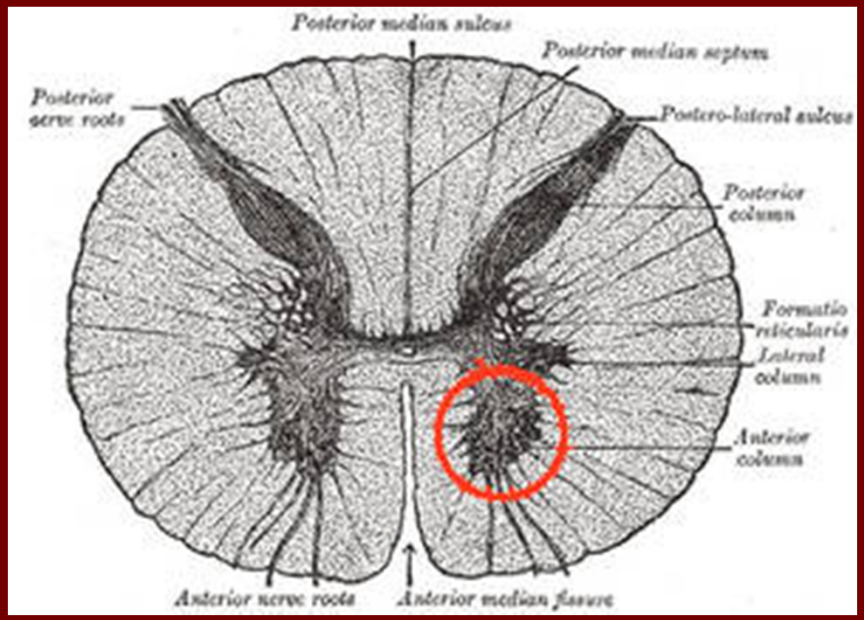
Spinal Muscular Atrophy

- “Infantile paralysis”
- Clinical signs during life:
  - Progressive weakness without spasticity; flaccid paralysis
  - Muscular atrophy present

Spinal Muscular Atrophy

- Anatomical findings at death:

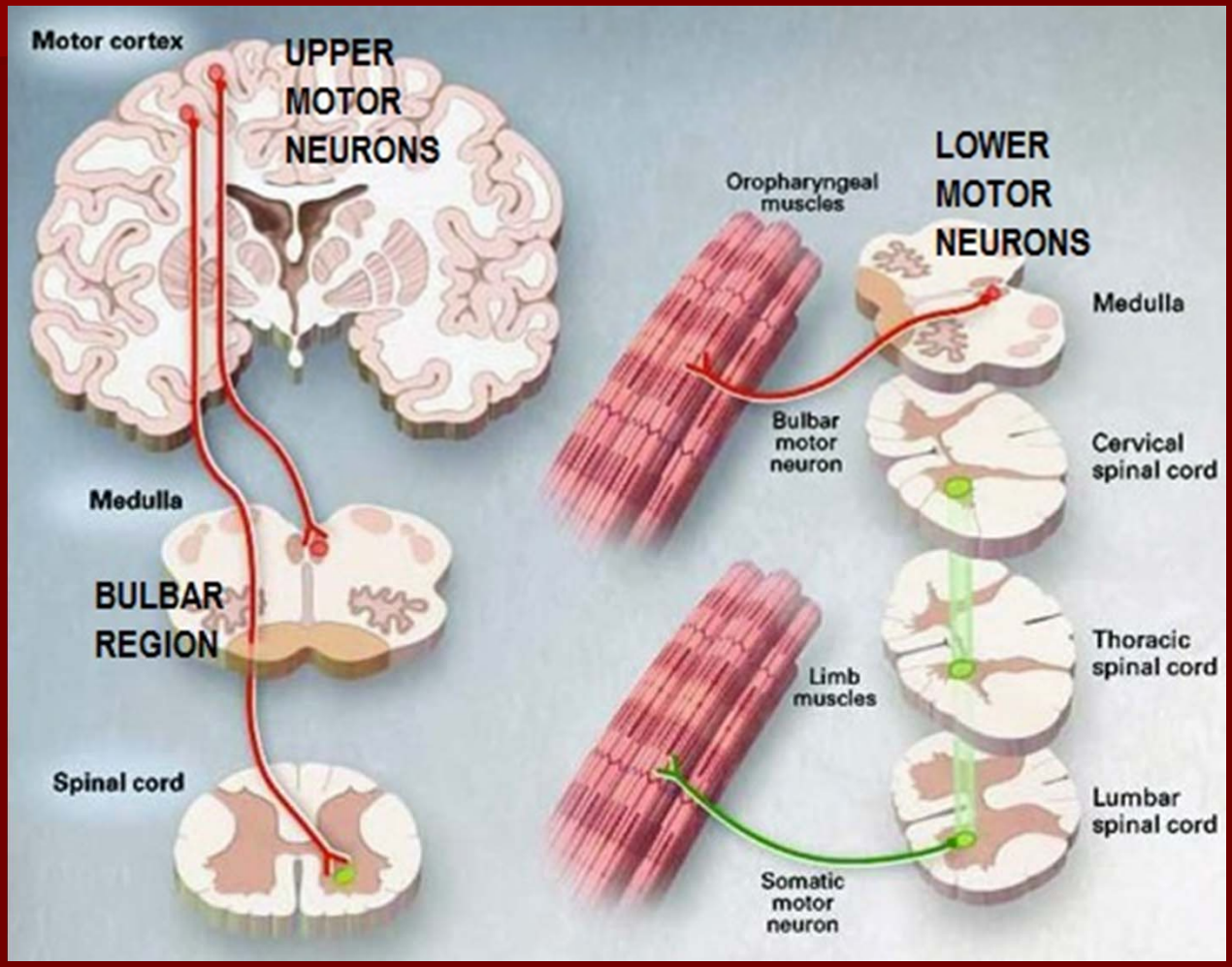
- Degeneration was limited to “anterior horn cells”
- Lateral columns & all white matter unaffected



2-part Motor System

- Motor system divided into two parts:
  - Damage to lateral columns of white matter, (now known as *lateral corticospinal tracts*) caused spastic weakness without atrophy
  - Damage to anterior horn cells causes flaccid weakness with muscle atrophy

Motor pathways



Sclérose latérale amyotrophique

- Some patients had progressive weakness with both spasticity and muscle atrophy
- Autopsy confirmed both parts of motor system affected
- Amyotrophic – muscle wasting from LMN pathology
- Lateral Sclerosis – spasticity from UMN pathology

Amyotrophic Lateral Sclerosis

- Progressive neurodegenerative disease which almost exclusively affects upper motor neurons and lower motor neurons
- In the U.S., best known as Lou Gehrig's Disease
- Outside U.S., called "motor neurone disease"

ALS Disease Course in 1860s

- "...from the first symptom to the fatal end . . . does not usually extend more than three years."
- Disease spreads from one extremity to the others, eventually to the brainstem-innervated "bulbar" muscles
- Death is typically due to respiratory failure, with or without pneumonia

Motor Neuron Diseases

- Primary Lateral Sclerosis (PLS)
  - Pure upper motor neuron dysfunction
- Amyotrophic Lateral Sclerosis (ALS)
  - Upper and lower motor neuron dysfunction
- Progressive Muscular Atrophy (PMA)
  - Pure lower motor neuron dysfunction
- also Spinal Muscular Atrophy (SMA)
  - Pure lower motor neuron disease, onset usually in childhood, hereditary

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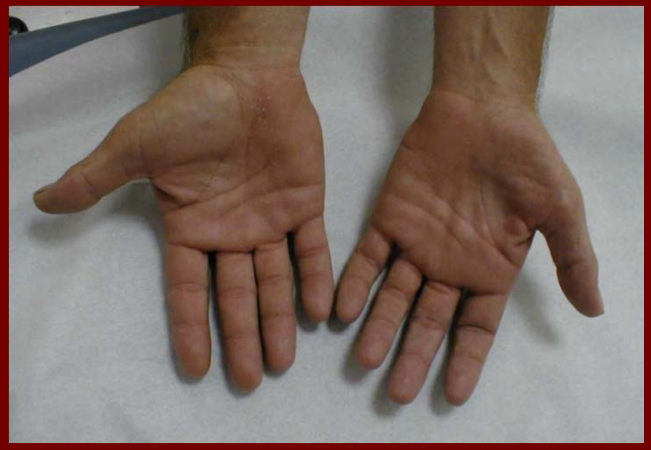
“Progressive Weakness”

- Progressing? How quickly?
  - Could be GBS or CIDP
- Fluctuating? Diplopia/ptosis?
  - Could be myasthenia gravis
- Sensory disturbance? Pain?
  - Could be radiculopathy or neuropathy
- Any recent illness?
  - Could be infectious; e.g., West Nile or Zika virus
- Bowel/bladder dysfunction?
  - Myelopathy

Physical Exam

- Evaluation should look for:
  - Upper motor neuron signs
    - Spasticity,hypertonia,hyperreflexia
  - Lower motor neuron signs
    - Fasciculations, atrophy
  - Symmetry vs. asymmetry
  - Length-dependent?
  - Sensory, autonomic, cognitive involvement?
  - Bulbar/respiratory muscle involvement?



Diagnostic Workup

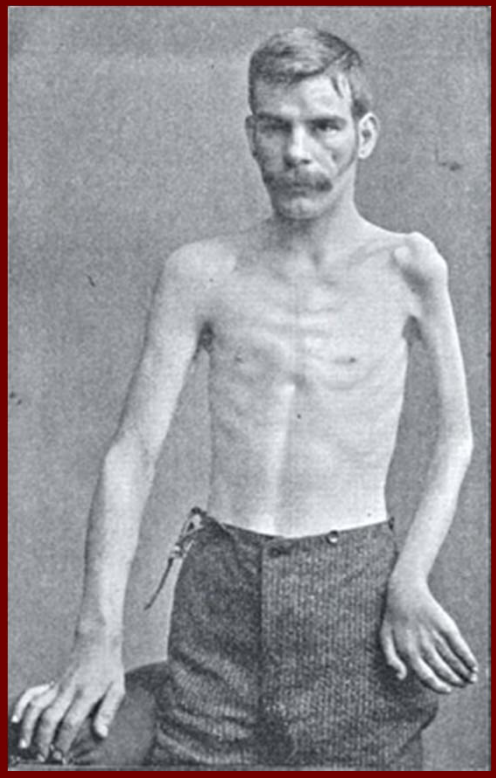
- PLS Mimics:
  - Myelopathy
    - compressive
    - neoplastic
    - infectious (HIV, HTLV-1)
  - Multiple sclerosis/transverse myelitis
  - Hereditary Spastic Paraparesis
  - Brainstem glioma
  - B12 deficiency

Diagnostic Workup

- ALS Look-alikes (not many):
  - B12 deficiency and copper deficiency can cause UMN and LMN symptoms, but usually with sensory symptoms
  - Myeloradiculopathy (compressive, syrinx…)
    - Myelopathy – UMN signs in legs (Babinski, clonus etc.)
    - Radiculopathy – LMN signs in upper extremity
    - Again, usually with sensory sx's, probably some incontinence, too

Diagnostic Workup

- PMA Look-alikes:
  - Multifocal motor neuropathy
    - Most important mimic of motor neuron disease
  - Diabetic and/or inflammatory amyotrophy (e.g., Parsonage-Turner syndrome)
  - Infectious (HIV, WNV, other enteroviruses)
  - Myopathy, inclusion body myositis
  - Myasthenic syndromes



Diagnostic Workup

- Neurodiagnostic testing
  - Nerve conduction studies
  - Electromyography
  - Neuromuscular ultrasound
- Serology based on DDx
- MRI (brain, C-spine, T-spine +/- L-spine)
- Genetic testing if FHx present or dementia

Zebras I have never seen (or recognized)

- SBMA (Kennedy's disease)
  - X-linked recessive, expanded CAG repeat on the androgen receptor gene
  - Gynecomastia
  - Proximal weakness
  - Early bulbar involvement
  - Prominent perioral fasciculations
  - Pure LMN involvement

Zebras I have never seen...

- Hexosaminidase A deficiency
  - Absolute deficiency results in Tay-Sachs disease
  - Partial deficiency results in “late-onset Tay-Sachs disease”
  - Abnormal metabolism>accumulation of gangliosides in neurons
  - LMN disease + cerebellar and/or psychiatric manifestations

Zebras are common in some parts of the world

- Human T-cell lymphotropic virus type 1 (HTLV-1): endemic in Caribbean
  - Tropical Spastic Paraparesis
  - Transmission sexual, transfusion or IVDA, maternal-fetal
  - Presentation similar to a predominantly motor transverse myelitis
    - Back pain, leg stiffness, urinary frequency

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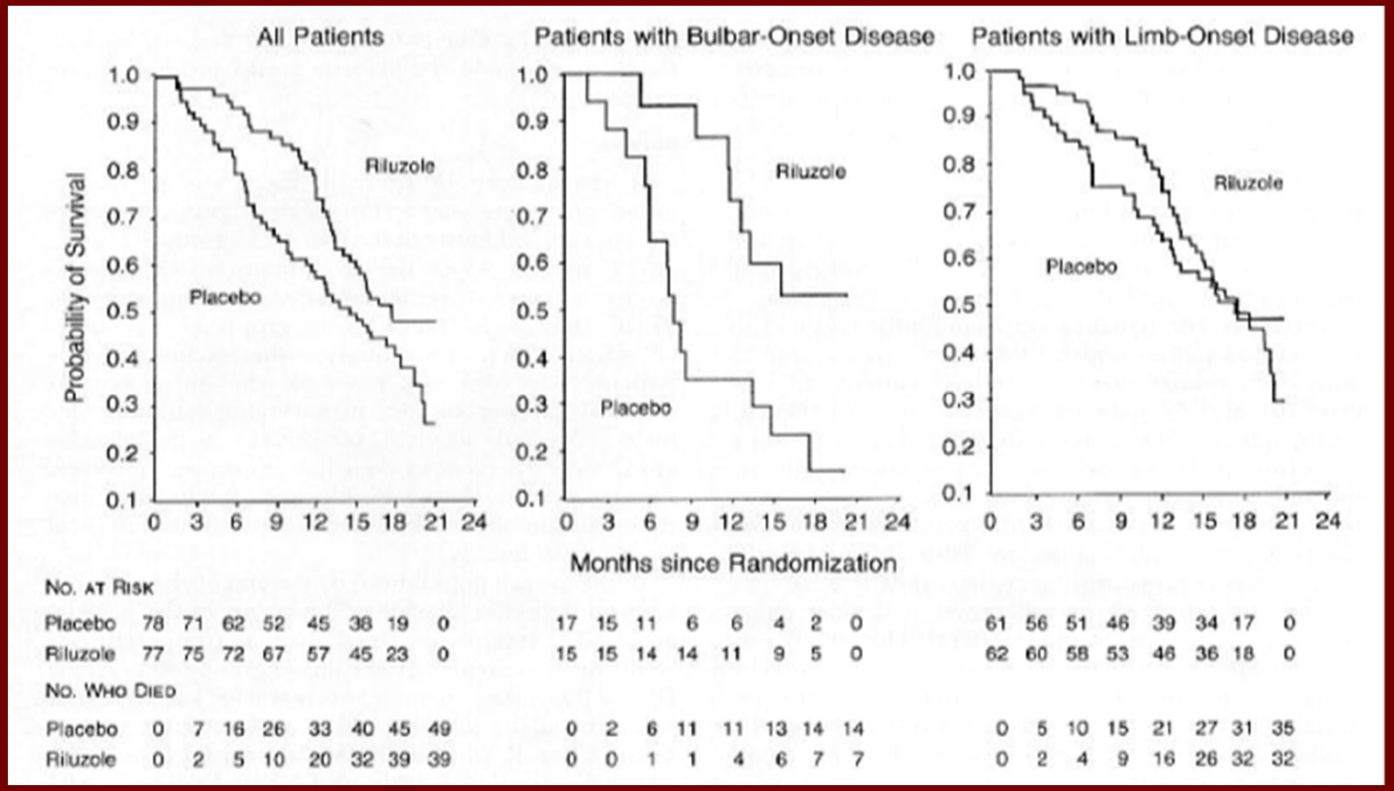
Breaking the news

- “My biggest concern is...”
  - “Survival is usually 3-5 years” from onset
- “I’m not 100% sure about this...”
- “I’d like to be wrong...”
  - 2nd opinion never unreasonable
- “There is a medication that slows the disease, but not by much...”

Riluzole in ALS

"Riluzole had a significant effect on rates of survival and muscular deterioration"



NEJM 330(9):585-91, 1994 Mar 3.

After diagnosis: more testing

- Pulmonary Function Testing
  - FVC, MIP, and MEP; SNIP if orofacial weakness
  - Possibly upright and supine
  - Nocturnal PSG with ETCO2 for hypopneas
- Swallow study
  - MBSS or FEES
- Nutrition assessment?

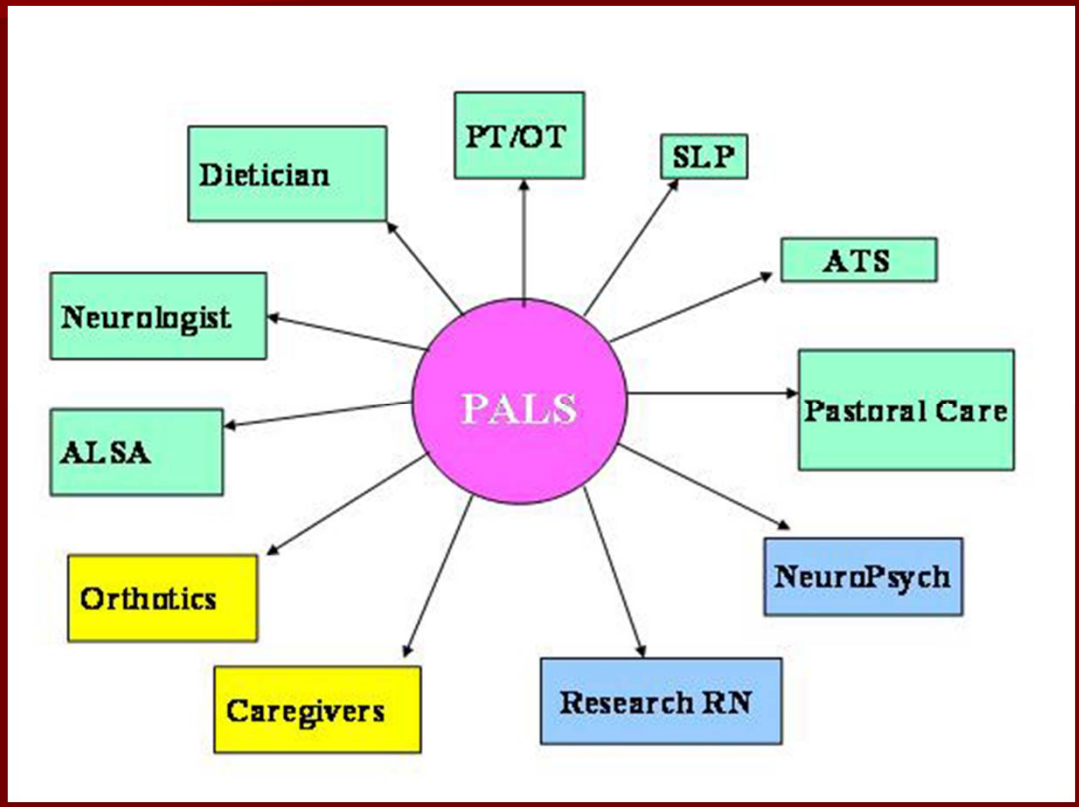
PEG and BiPAP

- Practice parameters published in 2009:
  - PEG should be considered to stabilize weight and prolong survival
    - Do you fatigue before you get full?
    - Consider PEG early; procedure has risks
  - NIV (BiPAP) should be considered in patients with respiratory insufficiency
    - To lengthen survival
    - To improve quality of life
    - Early initiation may increase compliance

More testing

- Neuropsychiatric screens
  - Cognition not always unaffected
  - Labile “pseudobulbar” affect common
  - Executive dysfunction not uncommon
    - May impact on treatment decisions/advance directives
- Speech evaluation
  - Dysarthria often largest barrier to treatment
  - Augmentative communication

The Multidisciplinary Clinic



"lifted" from the ALS Association St. Louis Regional Chapter

Goals of a Multidisciplinary Clinic

- More than a ‘one-stop shop’
- Improve patient care
- Improve communication
- Avoid omissions
- Avoid duplications
- Learn from and teach each other
- Participate in clinical trials

The Clinic Team

- Physician
- Clinic Coordinator
- Speech Therapist
- Respiratory Therapist/Pulmonary Rehab
- Occupational Therapist
- Physical Therapist
- Psychologist
- Social Services/case manager
- ALS Association

The Clinic Team

- Physician
  - Diagnosis
  - Guiding treatment
  - Medical therapies
    - Riluzole
    - Anticholinergics for sialorrhea
    - Medications for spasticity/cramping
    - Dextromethorphan/Quinidine (NueDexta) for pseudobulbar affect
    - Antidepressants?

The Clinic Team

- Clinic Coordinator/ALS Nurse
  - This is who is really in charge
  - Prioritizes clinic visit for each patient
  - Ensures that plans are carried out
  - Primary patient/family contact

The Clinic Team

- Speech Therapist
  - Dysphagia
    - Swallow evaluation
    - Safe swallowing techniques
    - When is PEG appropriate?
    - Home suction device?
  - Dysarthria
    - Optimize speech
    - Optimize communication – AAC evaluation?

The Clinic Team

- Respiratory Therapy/Pulmonary Rehab
  - Evaluate pulmonary function
  - Assist with NIPPV or similar
  - Mechanical in-/exsufflation?
  - Home suction device?
  - PPV vs. NPV?
  - Breath-stacking?

The Clinic Team

- Occupational/Physical Therapists
  - Preserving function in the setting of a progressive neuromuscular decline
  - Maintaining independence
    - Patient
    - Patient and caregivers
  - Appropriate bracing, stretching & exercise
    - Improving/maintaining function
    - Preventing contractures
  - Mobility evaluation when ambulation fails

The Clinic Team

- Psychology
  - Terminal illness: grief, anger, depression are common, but not always obvious
  - Pseudobulbar affect
  - Cognitive impairment – executive dysfunction
  - Family dynamics
- Social services
  - Resources: disability? transportation? disposition? Advanced directives?

ALS Association

- Encouraging, identifying, funding and monitoring worldwide ALS-directed research.
- Addressing the needs of ALS patients and the ALS community.
- Advocating for public policy in support of ALS-directed research and ALS-related healthcare issues.
- Promoting awareness and understanding of ALS and the role and work of The ALS Association.
- Developing, securing and managing resources necessary to grow and support the programs of The Association.

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Extending our clinic

- Problem:
  - Transportation, mobility, caregiver availability can all make a >3 hour clinic visit too difficult
  - Long Term Care residents are not eligible
- Solution:
  - Develop a community-wide network of healthcare providers familiar with motor neuron diseases.

Summary

- ALS and other motor neuron diseases suck
- Nothing stops the decline (yet)
- Some things can slow the decline
- Other things can improve quality of life
  - You can make a difference
  - It will change your life

Schedule of Events

- 8:00 Overview of Amyotrophic Lateral Sclerosis
  Martin Brown, MD
- 8:45 Respiratory Therapy Care in ALS
  Peggy Cox, RN, RRT
- 9:15 Speech Therapy Care in ALS
  Brittney Skidmore, MS, CCC-SLP
- 9:45 Panel Discussion
- 10:00 Break
- 10:30 Physical Therapy Care in ALS
  Kathy Paper, PT, MSPT
- 11:00 Occupational Therapy in ALS
  Scott Burgener, OTR/L
- 11:30 Psychological Services in the patient with ALS
  Courtney Smith, PhD
- 12:00 Panel Discussion
- 12:30 Evaluation and Adjournment

Let’s kick some ALS!!!