Amyotrophic Lateral Sclerosis (ALS)

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BUMC

- It is a relentlessly progressive disease of the Motor System
- Commonly known as Lou Gehrig’s Disease
- Called Motor Neuron Disease in Britain
- A relatively uncommon disorder
- Incidence 1.8/100,000 population
- Prevalence of 2-7/100, 000 population

The ‘iron horse’

History

History

- First described by Charcot in 1869

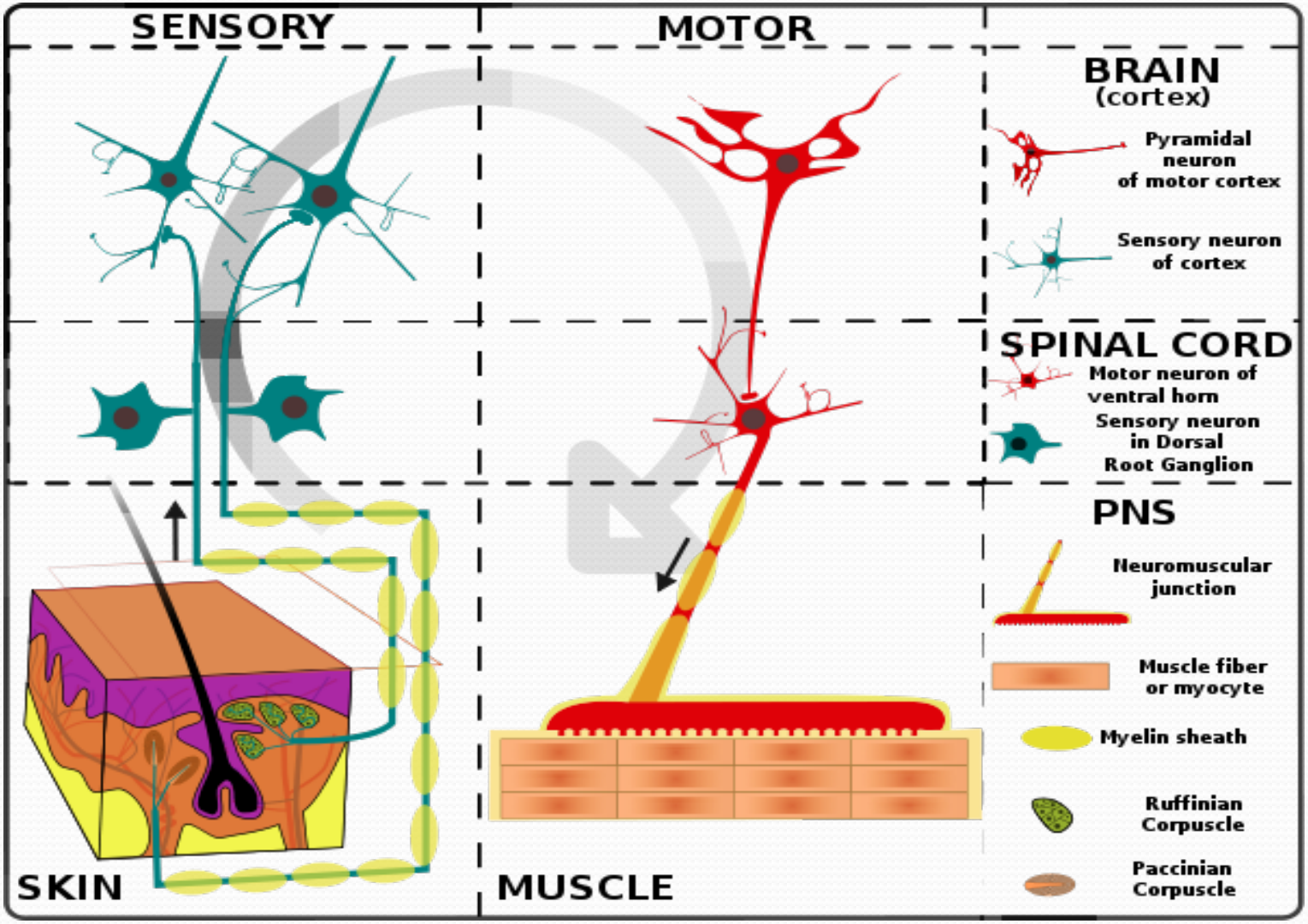
- The science of ALS, however, remained largely descriptive
- In 1990 World Federation of Neurology met in El Escorial, Spain and published the diagnostic criteria for ALS
- The EE criteria was considered too restrictive and was relaxed in 1998

- The first breakthrough came in 1991
- Teepu Siddique et al, at Northwestern University Chicago, identified the 1st genetic mutation causing ALS in some families
- Superoxide dismutase gene on chromosome 21

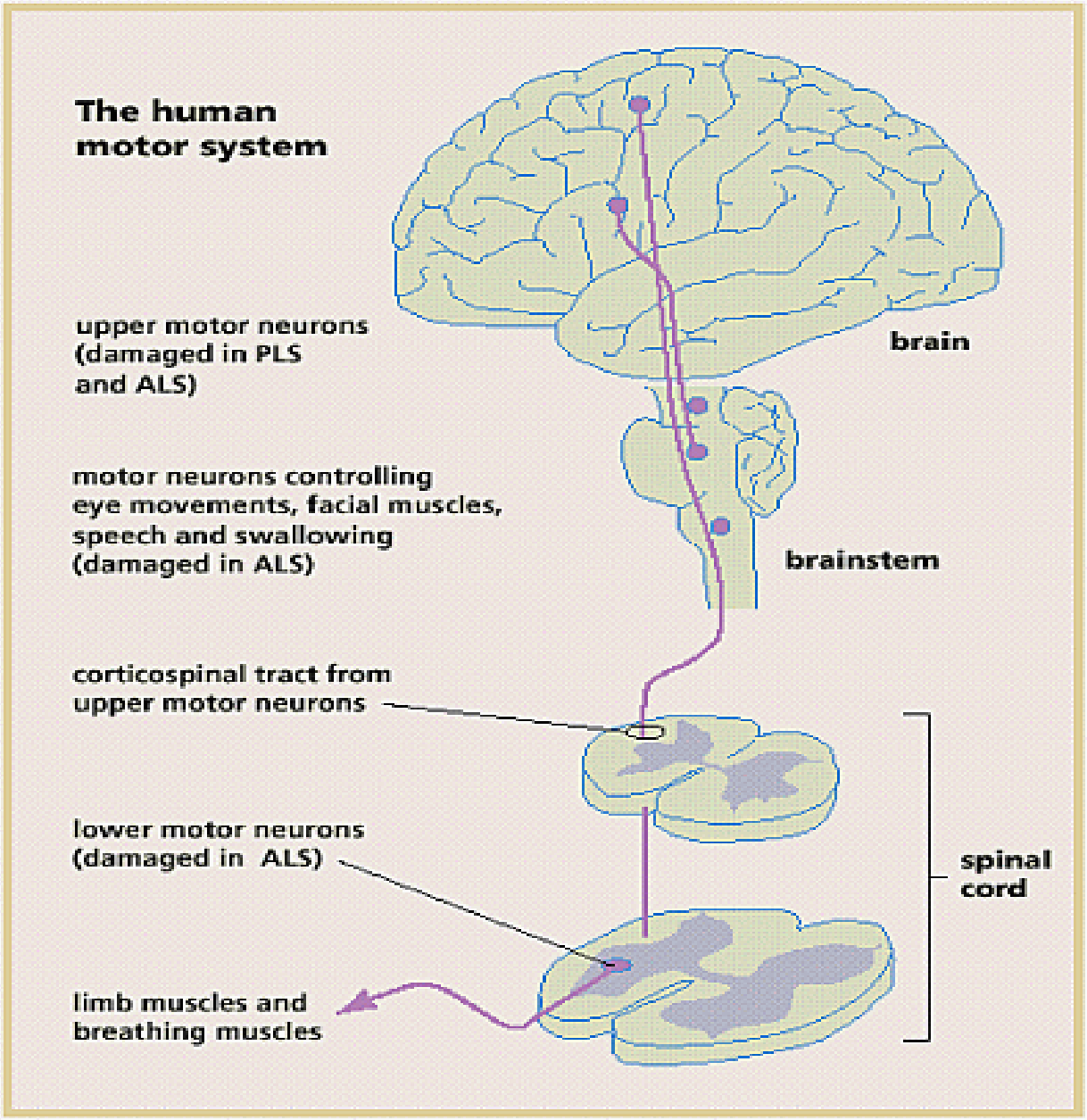
- This led to the development of animal models of ALS and the ability to rationally develop and test drugs for ALS
- In 1994 Riluzole was reported to prolong survival in ALS (Bensimon et al)
- Multiple other genetic mutations have since been identified in familial ALS

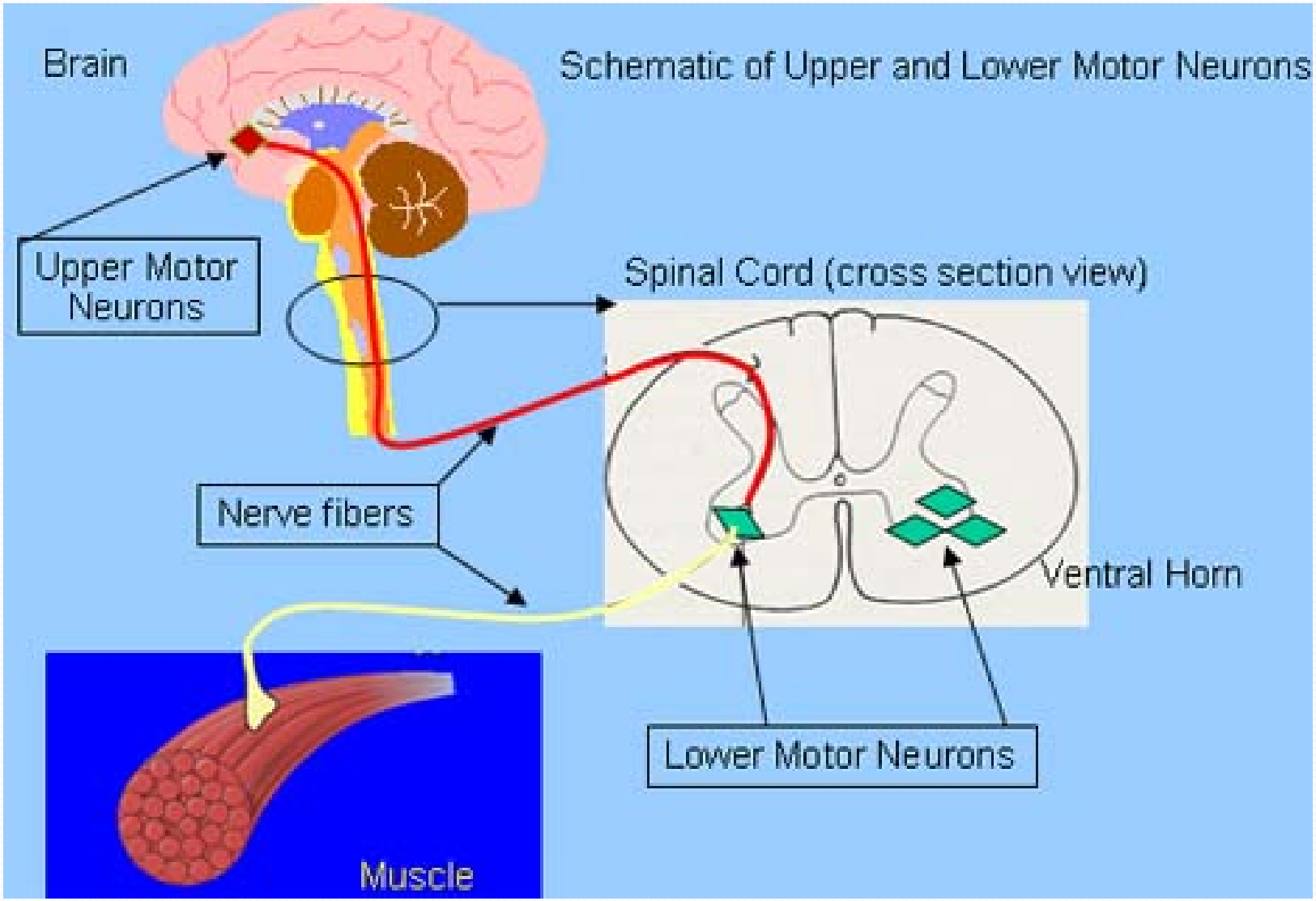
Nervous System

How is the Nervous System organized?



What is in the motor system?


The human
motor system
upper motor neurons
(damaged in PLS
and ALS)
brain
motor neurons controlling
eye movements, facial muscles,
speech and swallowing
(damaged in ALS)
brainstem
corticospinal tract from
upper motor neurons
lower motor neurons
(damaged in ALS)
spinal
cord
limb muscles and
breathing muscles


Brain
Schematic of Upper and Lower Motor Neurons
Upper Motor Neurons
Spinal Cord (cross section view)
Nerve fibers
Ventral Horn
Lower Motor Neurons
Muscle

- Lower motor neuron (LMN) signs:
  - Weakness, muscle wasting, hyporeflexia, muscle cramps, fasciculations, weakness
- Upper motor neuron (UMN) signs:
  - Spasticity, hyper-reflexia, weakness

Epidemiology

Epidemiology

- Incidence 1.8/100,000 population
- Prevalence of 2-7/100, 000 population
- In the United States, about 7000 new cases of ALS are diagnosed each year
- 90% of cases are sporadic
- 10% are familial (FALS); most commonly autosomal dominant
- Male:Female – 1.4: 1
- Average age at onset is ~ 60 years
- Can start in teens or >75yrs

What is the cause of S-ALS?

- Glutamate excitotoxicity
- Free radical injury
- Neurofilament and Microtubule dysfunction
- Ubiquilin2 (*which is involved in recycling damaged and misformed proteins in key nerve cells*). In people with ALS, ubiquilin2 does not do this effectively, leading to an accumulation of the damaged proteins and ubiquilin2 in critical nerve cells in the spinal cord and brain (Nature 2011)

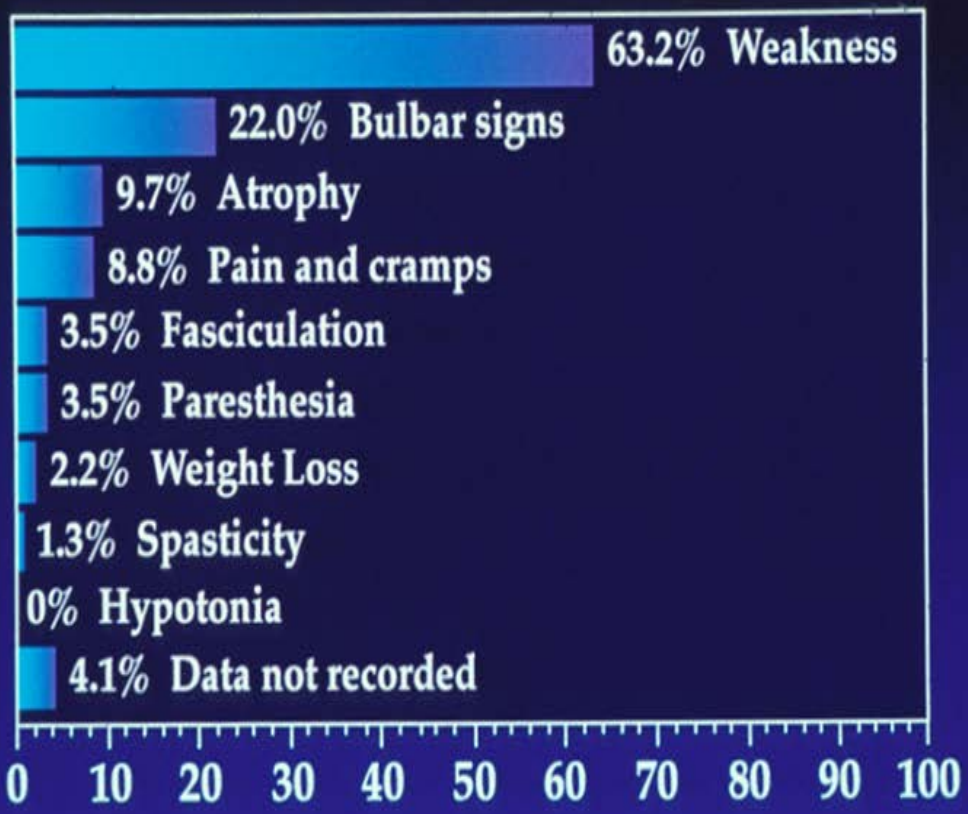
How do patients present?

- Patients present with a combination of upper and lower motor neuron signs

ALS DIAGNOSIS

Clinical Picture

Signs and symptoms at initial presentation

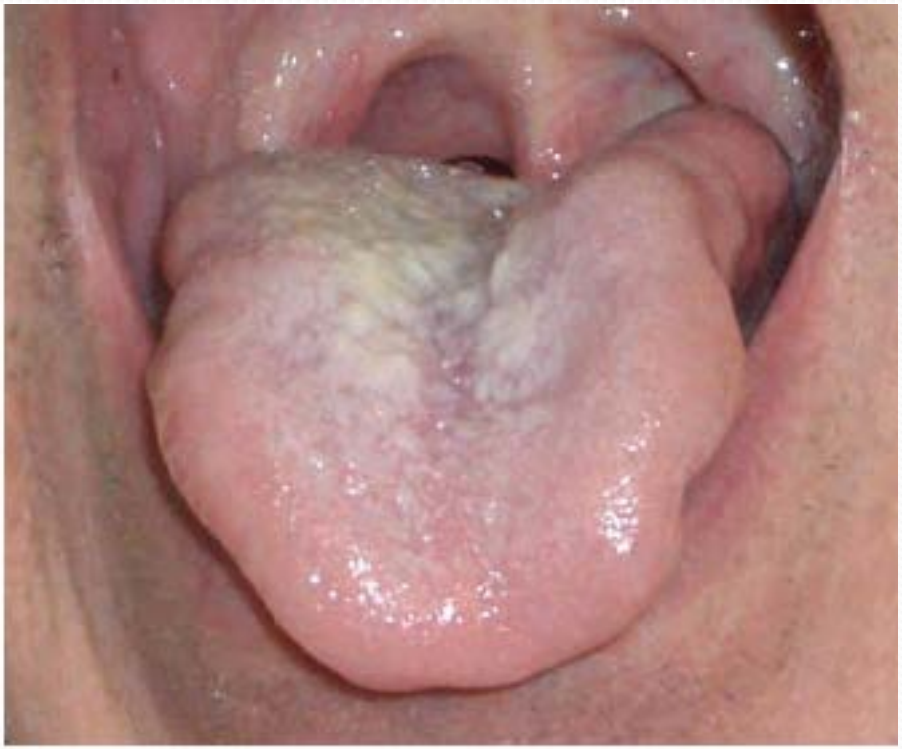


Clinical patterns at presentation

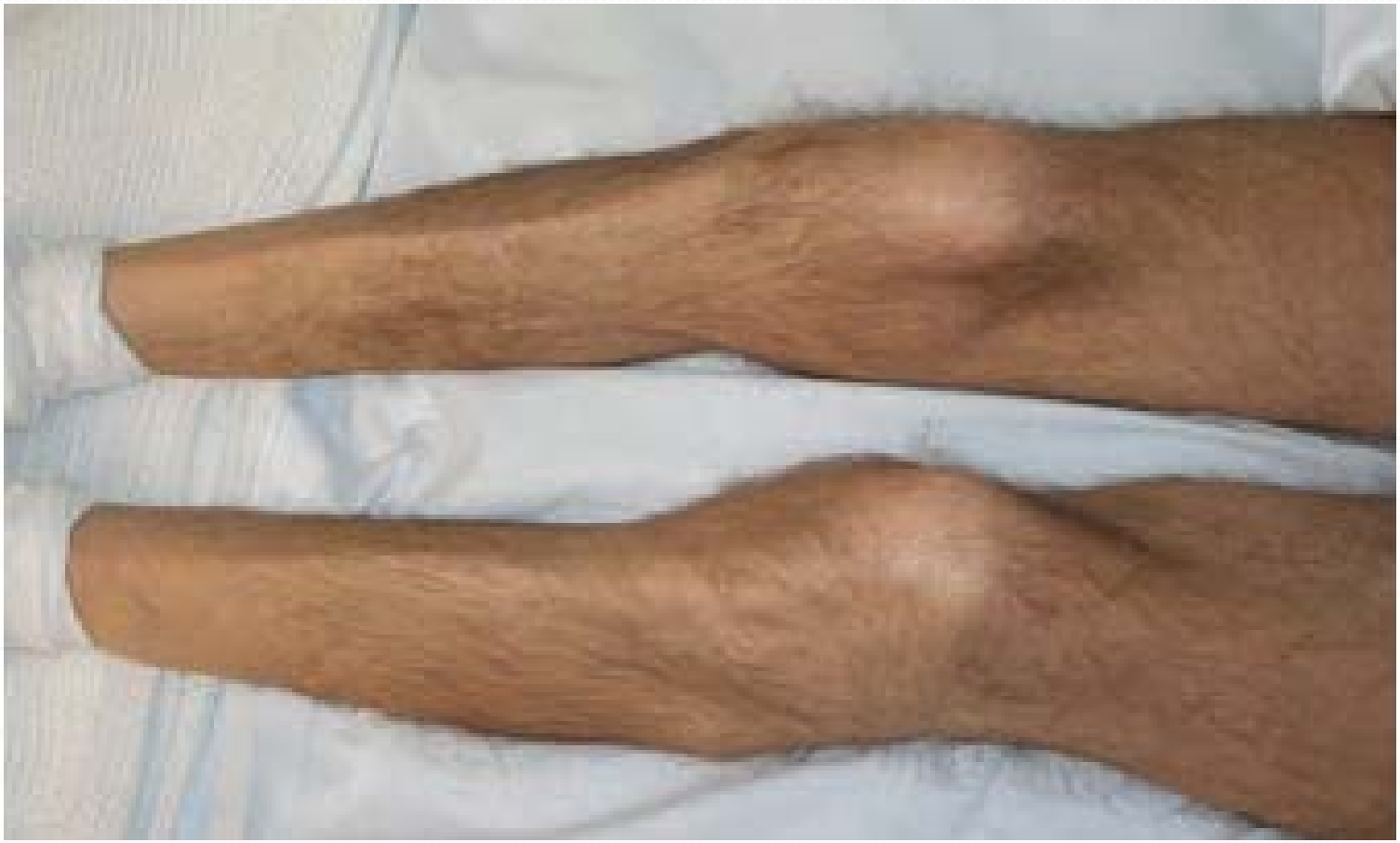
- Progressive bulbar palsy
- Progressive Muscular Atrophy
- Primary lateral sclerosis
- ALS (UMN + LMN)

- These patterns then progressively merge to develop full blown ALS picture (UMN + LMN)

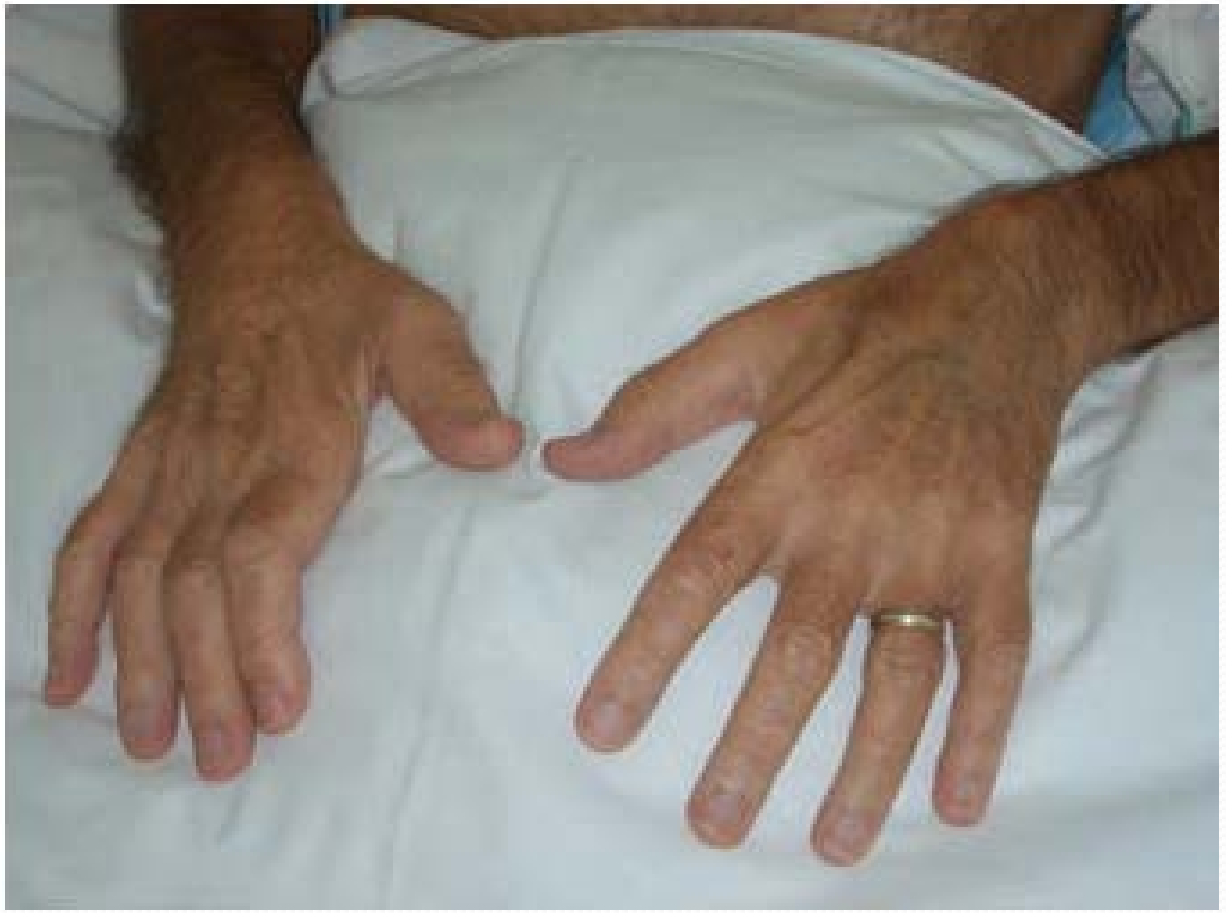
Tongue atrophy



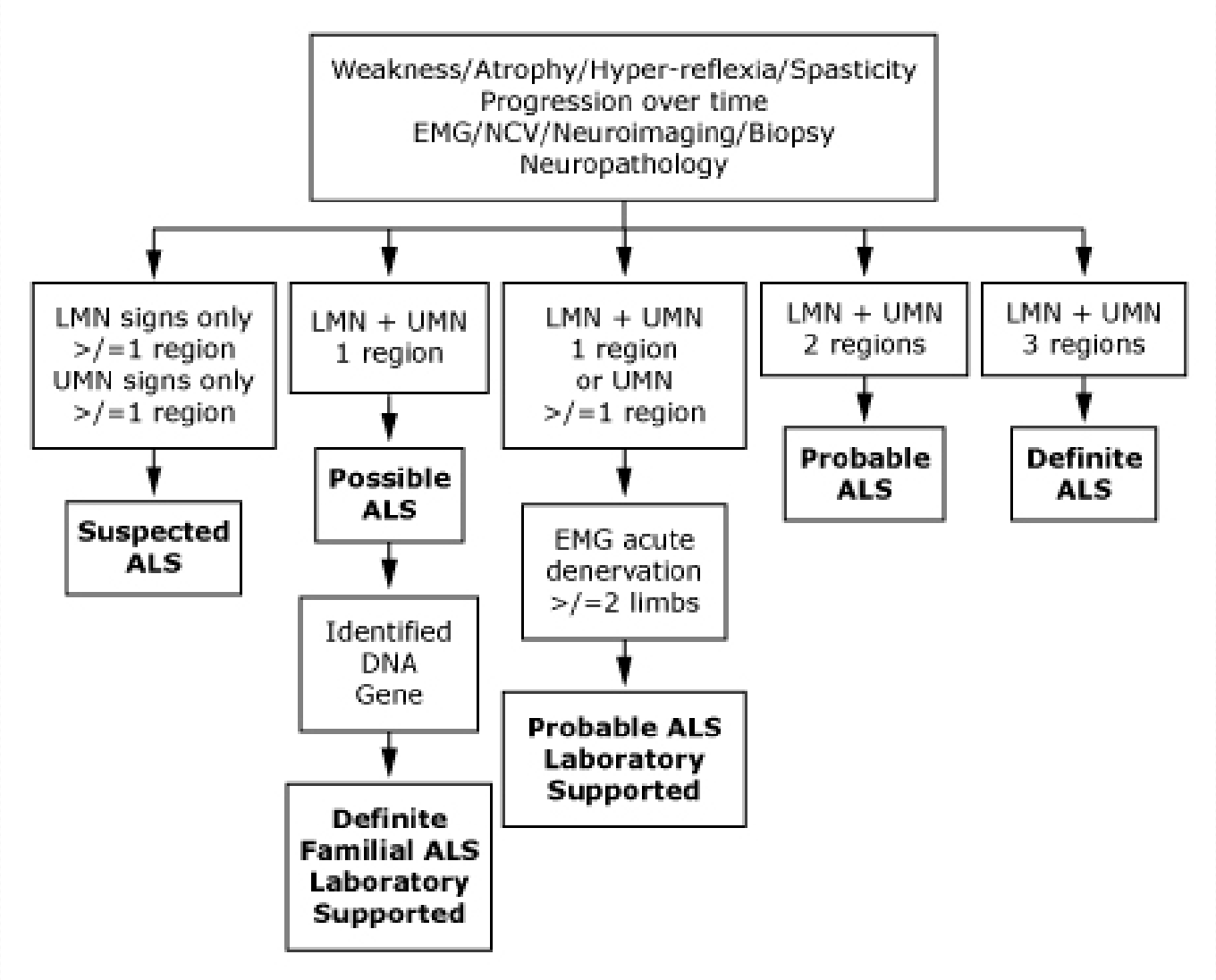
Leg wasting



Hand atrophy



El Escorial criteria



Prognosis

- Mean survival from onset is 23-43 months
- 5-yr. survival rate of 22%
- 10-yr. survival rate of 9.4%
- Poor prognostic factors:
  - Age >65 yr
  - Rapid disease progression
  - Dyspnea at onset
  - Rapid decline in pulmonary function

Can any tests help in diagnosis?

- There is no blood marker of S-ALS
- Diagnosis depends on the clinical picture
- EMG can be helpful by showing characteristic findings: fibrillations, fasciculations, reinnervation motor units
- Blood tests and imaging can help rule out other diseases

Treatment

Multidisciplinary Approach

- Neurologist
- Clinical/research nurse
- Dietician
- Speech/swallowing therapist
- Family/caregivers
- Psychologists
- Physical therapist
- Occupational therapist
- Social worker
- GI physician
- Support organizations
- Homehealth/hospice
- Pulmonologist

Phramacotherapy - specific

- Riluzole was approved in 1996
- It acts as an antiglutamate agent
- Median prolongation of survival of 2 months

Phramacotherapy - symptomatic

- Fatigue: pyridostigmine, SSRIs, Amantadine
- Spasticity: Baclofen, Tizanidine
- Cramps: Quinine, Clonazepam
- Psedobulbar affect: Dextromethorphan/Quinidine, SSRIs,
- Depressions: SSRIs, TCAs,

Speech and Communication

- Speech therapists to be involved early
- Introduce energy conserving skills
- Introduce non-verbal techniques
- Introduce assistive and augmentative devices

Respiratory care

- Goals and limitations of any intervention should be discussed in detail
- Non-invasive Positive Pressure Ventilation is used
- Generally offered when FVC <50%, patient is short of breath or when symptomatic hypercapnia occurs

Thank you