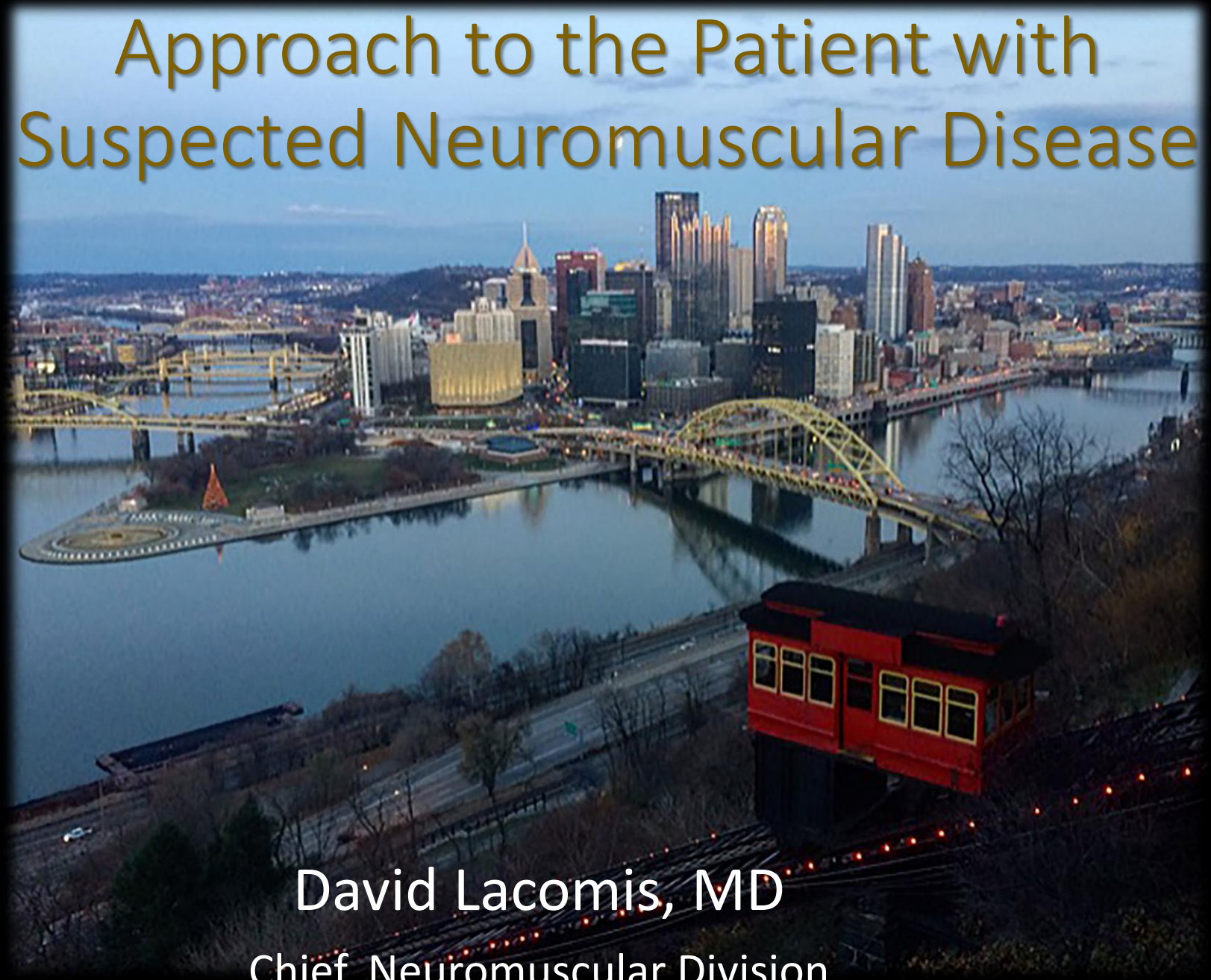
Approach to the Patient with Suspected Neuromuscular Disease



David Lacomis, MD

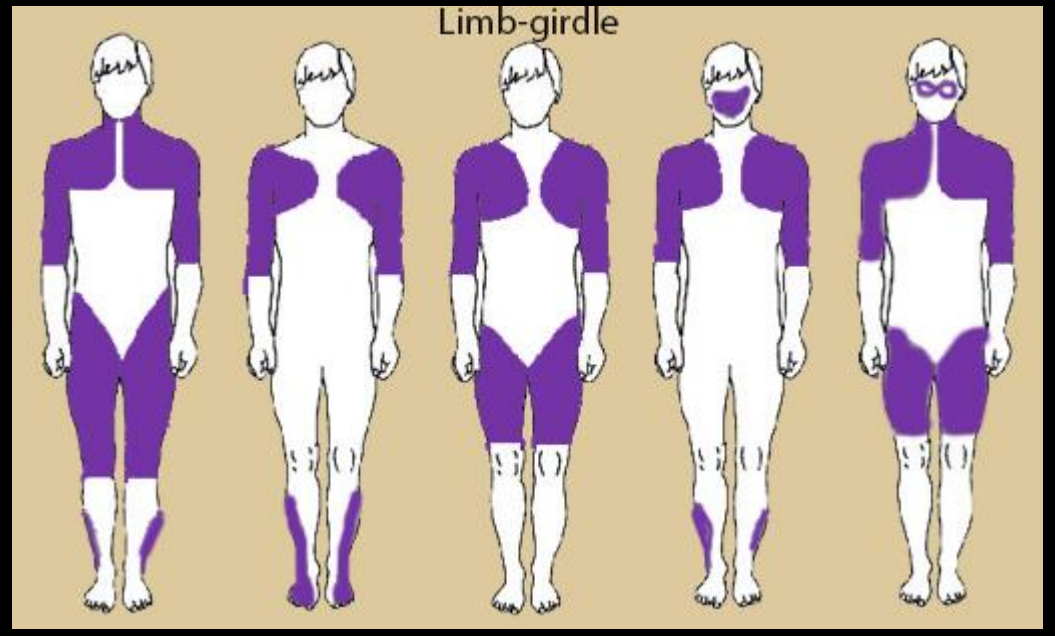
Chief, Neuromuscular Division

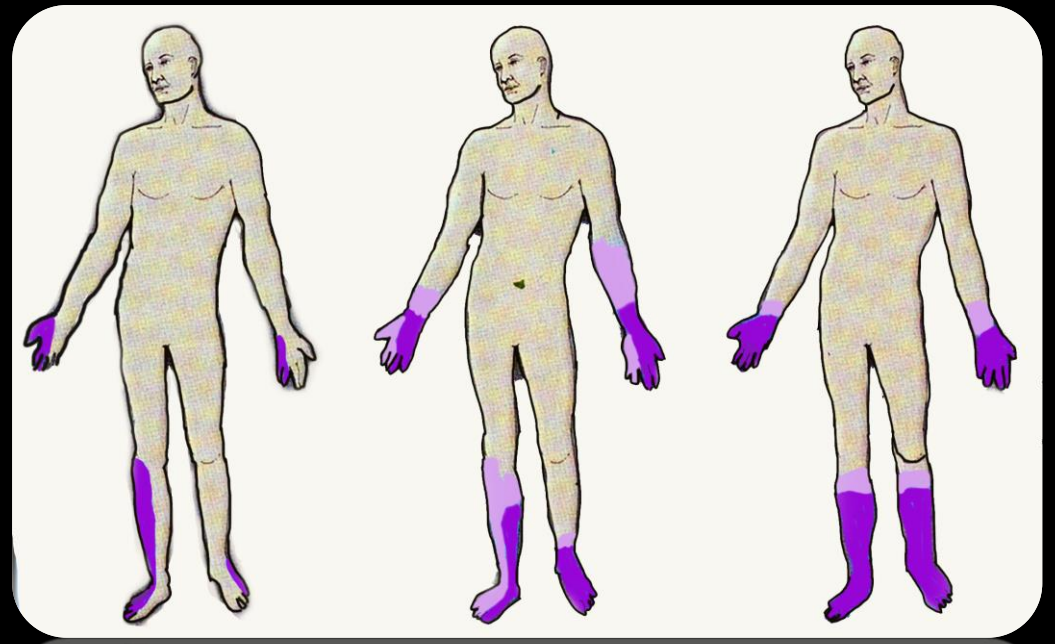
Goals

- Approach to NMD based on
  - Major Symptoms
  - Localization
    - Motor neuron, Peripheral Nerve, NMJ, Muscle
- Differential Diagnosis
- If you want …..to Initiate the Evaluation
  - Urgency

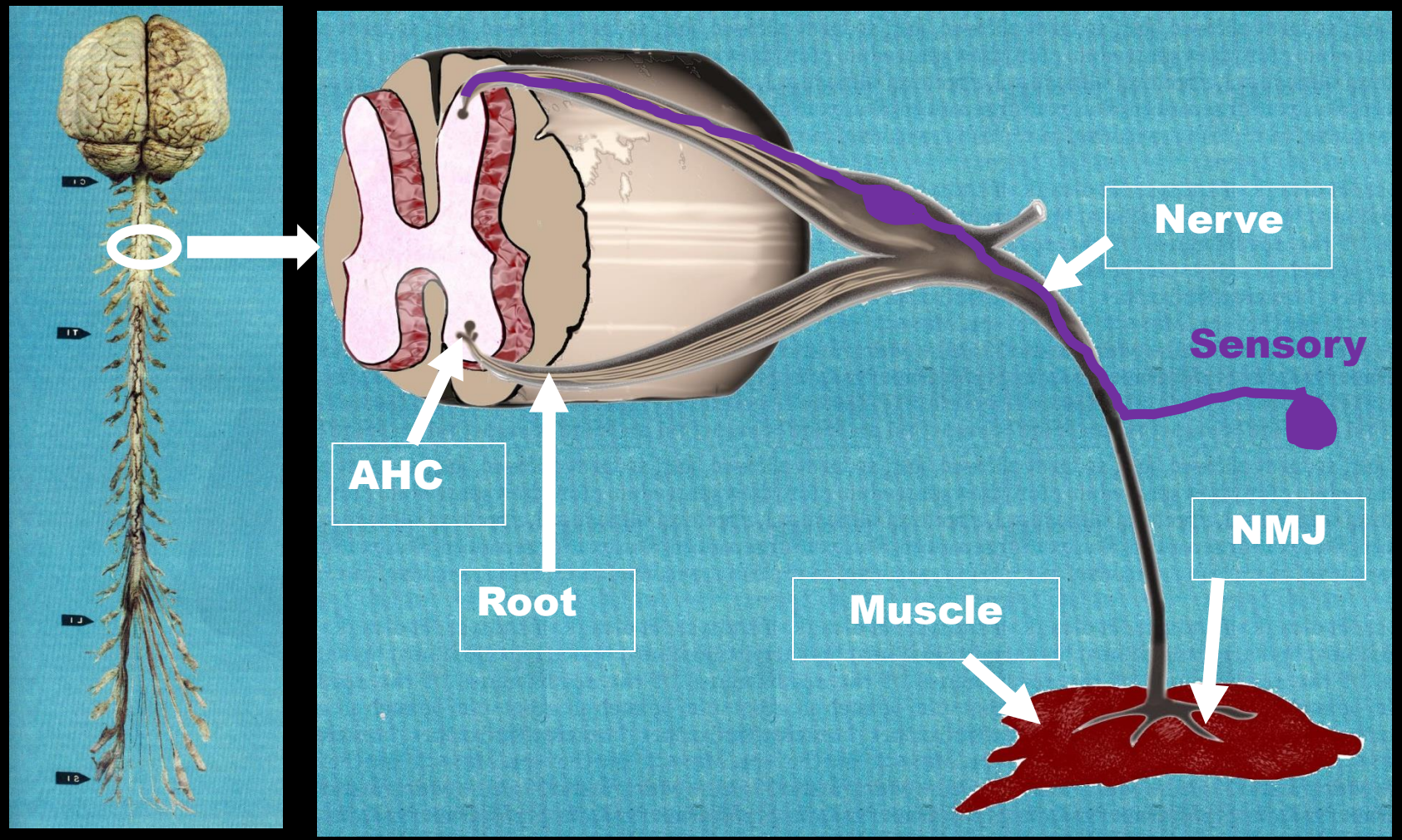
Major Symptoms

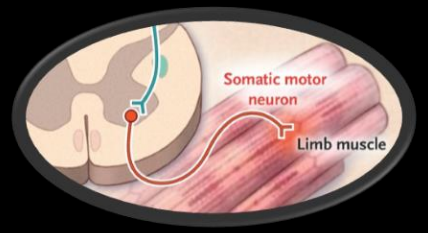
- Weakness
  - Patterns
- Paresthesias
  - Positive
  - Negative
- Other
  - Ocular
  - Bulbar
  - Respiratory
  - Cramp, twitch
  - Imbalance



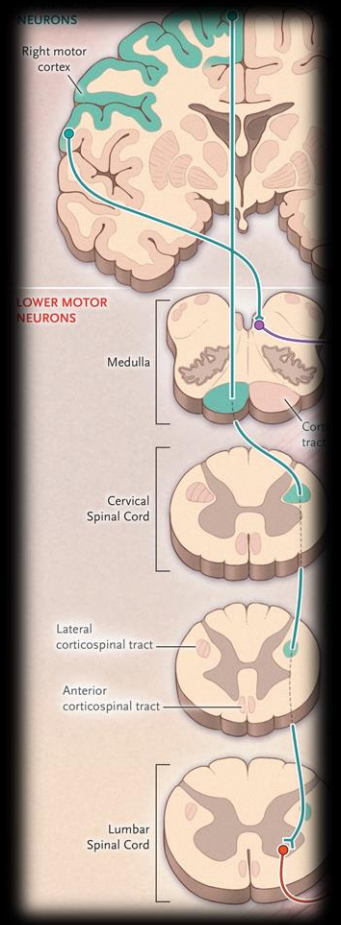


PNS- Localization





Motor Neuron Disease (ALS)



LOWER MOTOR NEURON LOSS

- WEAKNESS (painless): Limbs, Bulbar
- Asymmetry
- Loss of muscle mass (amyotrophy)
- Reduced reflexes
- Fasciculations

BRAIN MOTOR NEURON LOSS

- WEAKNESS WITH SPASTICITY
- Stiff, clumsy, Inc reflexes
- Emotional lability
- Dementia 10%

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Suspect Motor Neuron Disease (ALS)

Consult
Electromyography
Imaging

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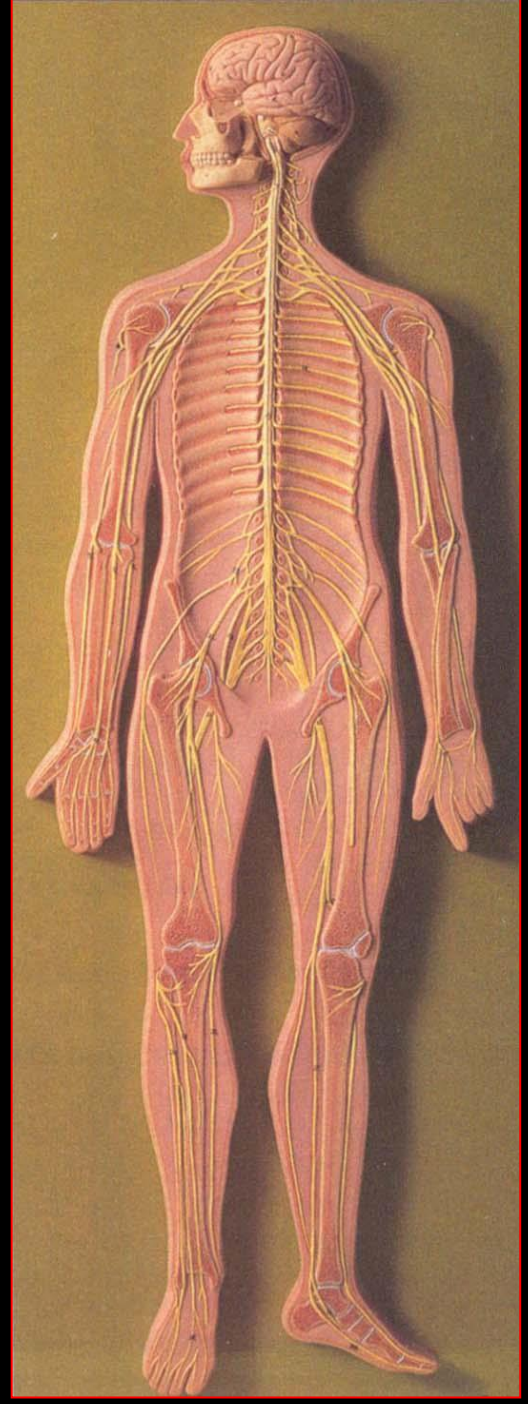
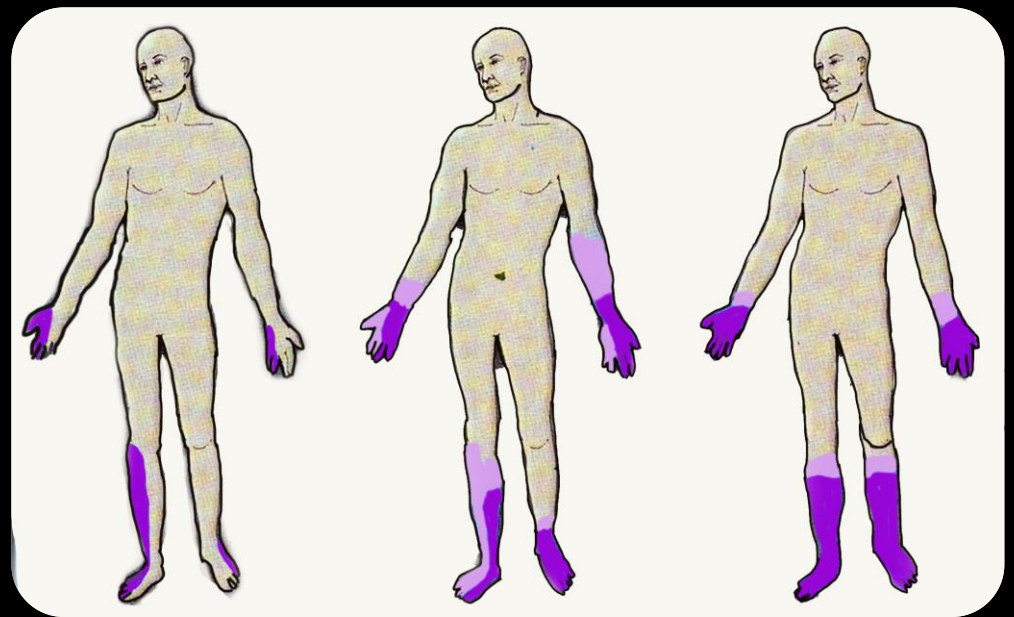
Distribution of Neuropathy

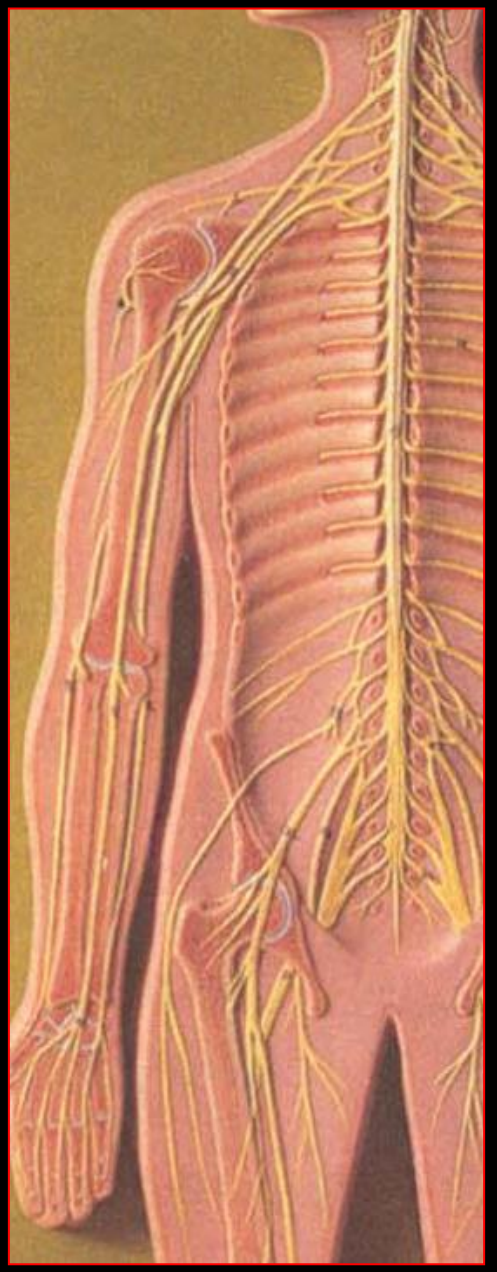
- Nerve roots (radiculopathy)
- Brachial plexus (plexopathy)
- Single nerve (mononeuropathy)
- Multiple nerves (mult. mononeuropathies)
- Diffuse (polyneuropathy)



Symptoms of Neuropathy

- Pain
  - Root, Plexus, Periph nerve
- Numbness
- Imbalance (proprioception)
- Weakness
- Dry mouth, dry eyes, lightheadedness, constipation, nausea, incontinence, ED
  - Dysautonomia/peripheral nerve

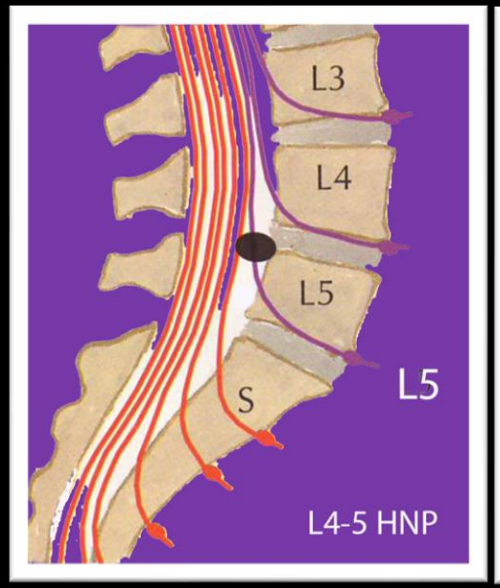


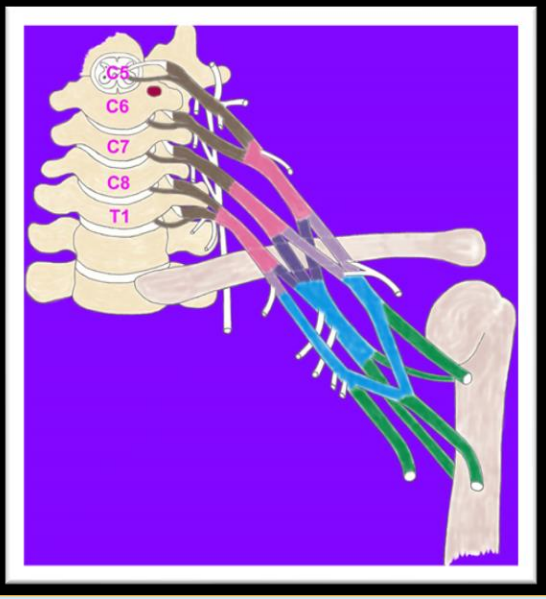


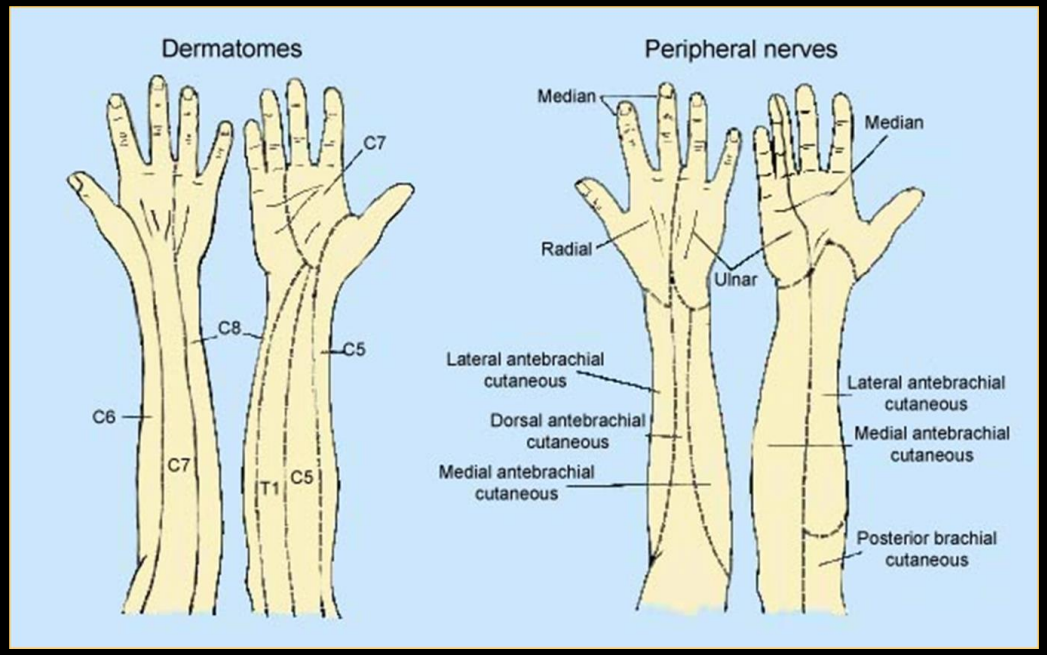
Evaluation of Neuropathy

- Root- imaging; occas EMG
  - Nonstructural
    - Lyme, sarcoid, viral, CA
- Plexus- EMG, imaging, consult
  - Neuralgic amyotrophy/Parsonage-Turner
  - Trauma, DM, hepE, infiltrative, Lyme, vasculitis
- Mononeuropathy –EMG

  DM, Arthritis, hypothyroid, trauma

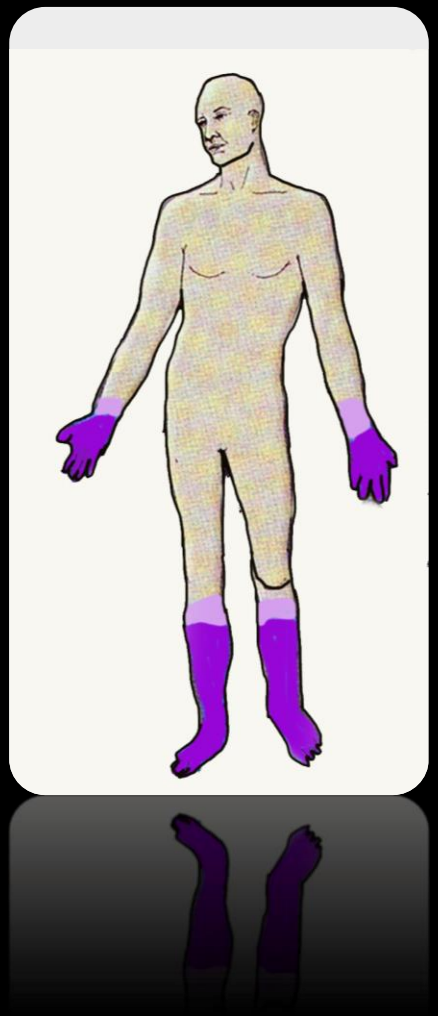






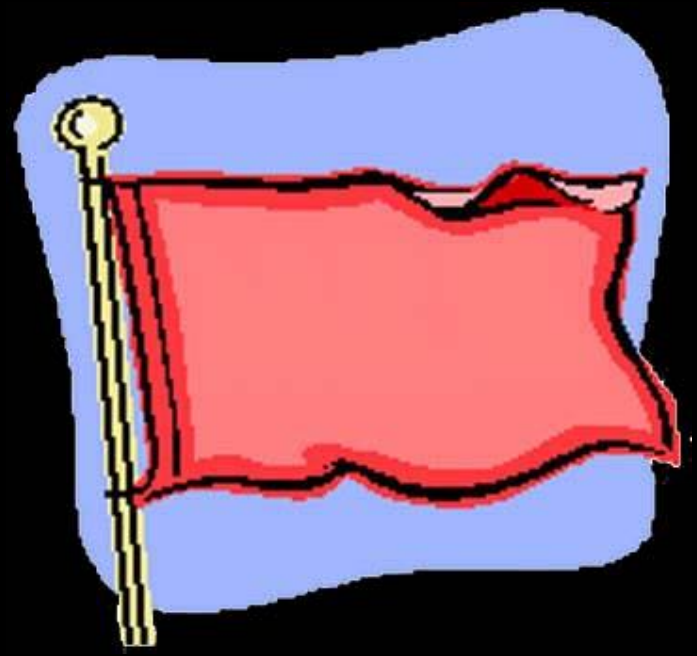
Evaluation of Polyneuropathy

- Symmetric, length-dependent, Axonal Sensorimotor
- Unknown cause-
  - EMG/NCS
  - Screen for diabetes, TFTs, B12, folate, SPEP with immunofixation and serum light chains
  - Treat or Consult



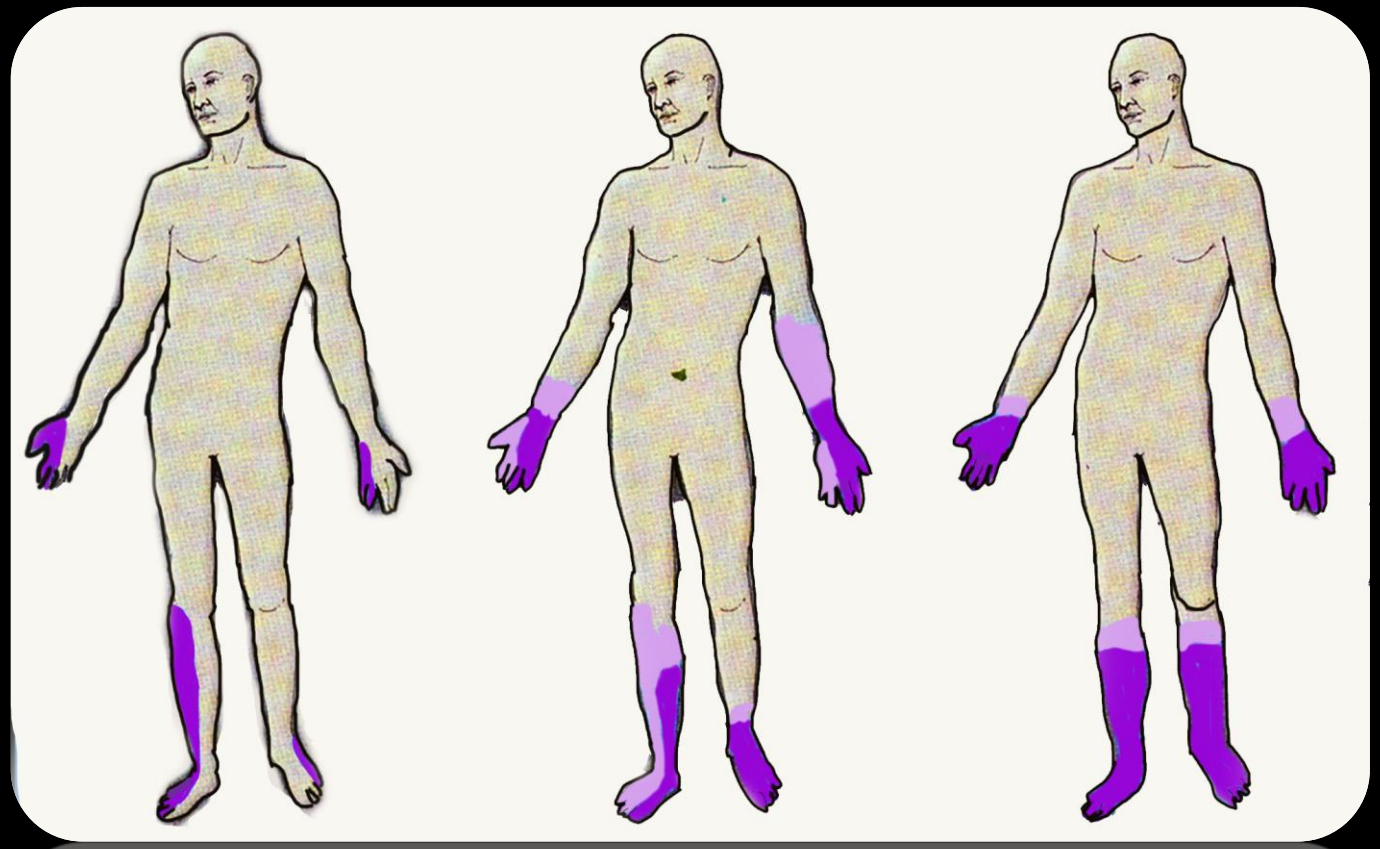
Diabetic with Neuropathy: Red Flags

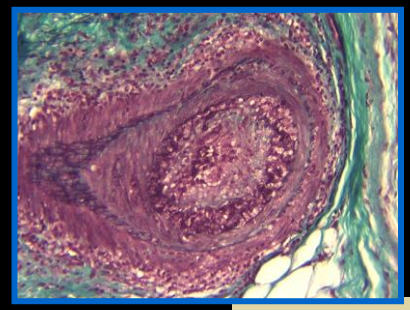
- Rapid PN course
- Course out of proportion to disease
- Asymmetry
- Early UE involvement
- Marked reflex loss
- Motor without sensory
- Worsens despite good Rx of metabolic syndrome



Vasculitic Polyneuropathy

True Multiple Mono-neuropathy	Overlapping (Extensive) Multiple Mono-neuropathy	Distal Symmetric Poly-neuropathy*
10-15%	**50-60%**	**25%**





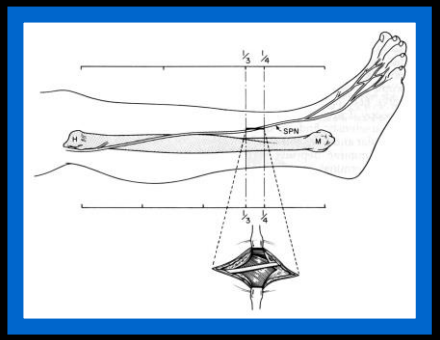
Eval

CTD screen

Consult

EMG/NCS

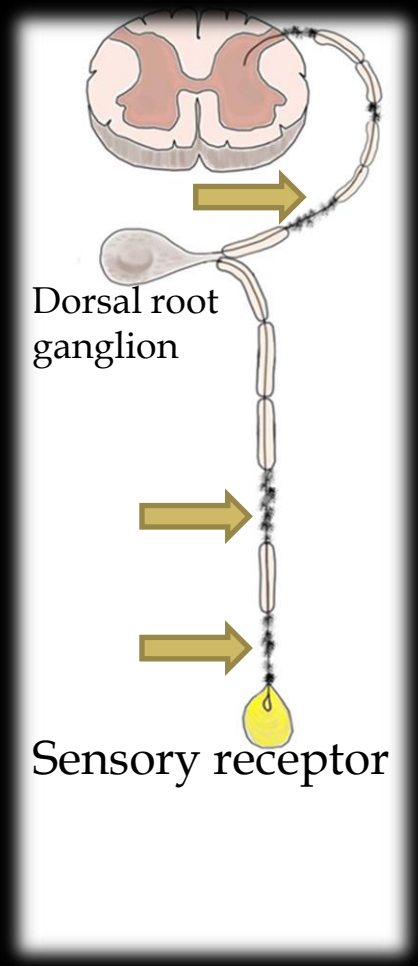
Biopsy*



*risk fxs?

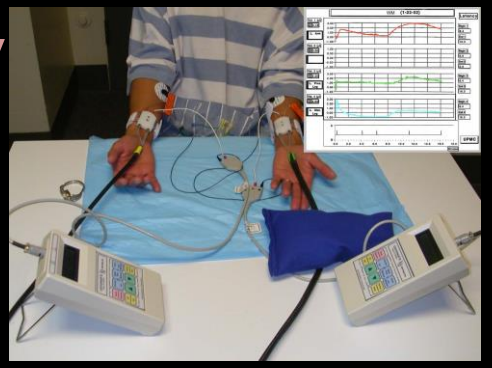
Demyelinating Polyneuropathy

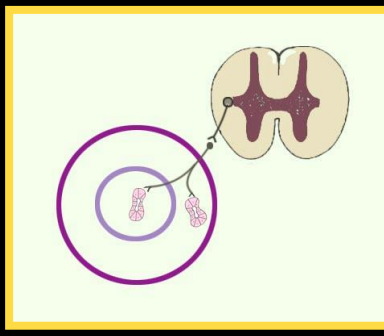
- Symmetric or rarely asymmetric, length-dependent or NOT
- Areflexia, large fiber > small fiber sensory sxs
- Rapid- GBS….emergency
- Subacute to Chronic
  - EMG/NCS
  - Screen for paraproteinemia
  - Consult

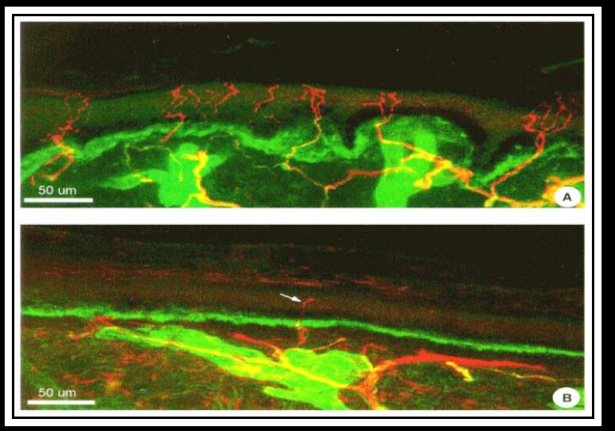


Evaluation of Polyneuropathy

- Painful Small fiber sensory neuropathy
  - FBS, HbA1c- OGTT if neg
  - Normal Nerve Conductions
  - Probably consult
- Prominent Dysautonomia
  - DM, amyloid including TTR mutation
  - autoimmune







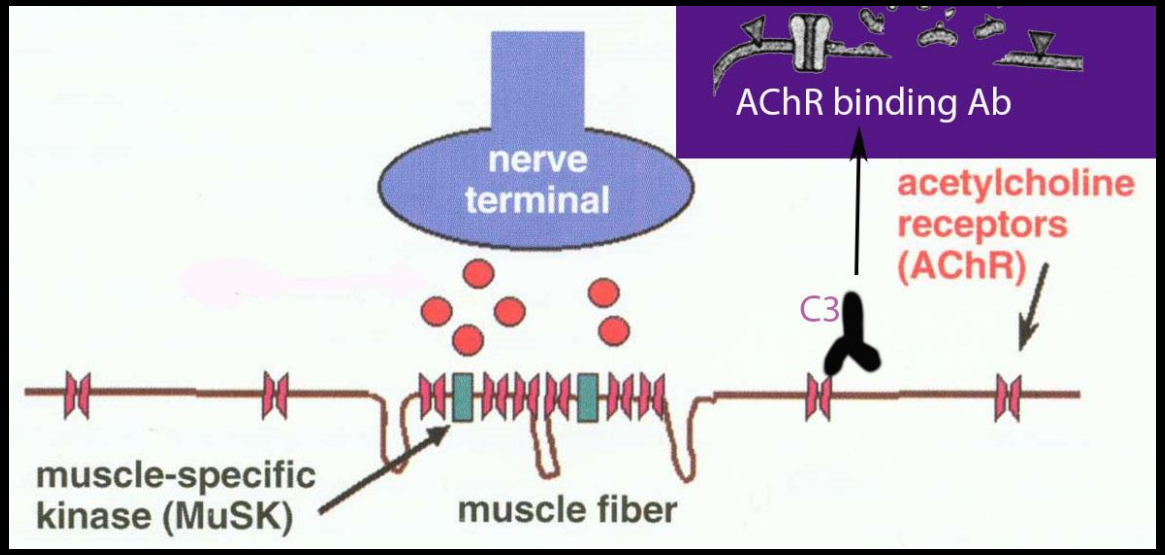
Periquet MI, et al. Neurology 1999;52:1641-1647.

Neuromuscular Junction

- Ocular Muscles- ptosis, diplopia
  - Pupil-sparing x botulism
- Face
- Bulbar, SOB
- Limbs, Neck (Painless)
  - *May be Asymmetric*
- *Fluctuates*
- *Better with cold*
- Autonomic with LEMS (dry mouth) + dec reflexes with LEMS

Evaluation for Myasthenia Gravis

- Acetylcholine Receptor binding Ab or get the MG Panel (AChR binding, blocking, & modulating Abs)
  - 85%+ in genl MG
- Reflex to MuSK Ab (in 50% of seroneg)
- Striated muscle Abs
- Consult
  - EMG/NCS
  - Chest CT



Myasthenia Gravis: Ice Bag Test

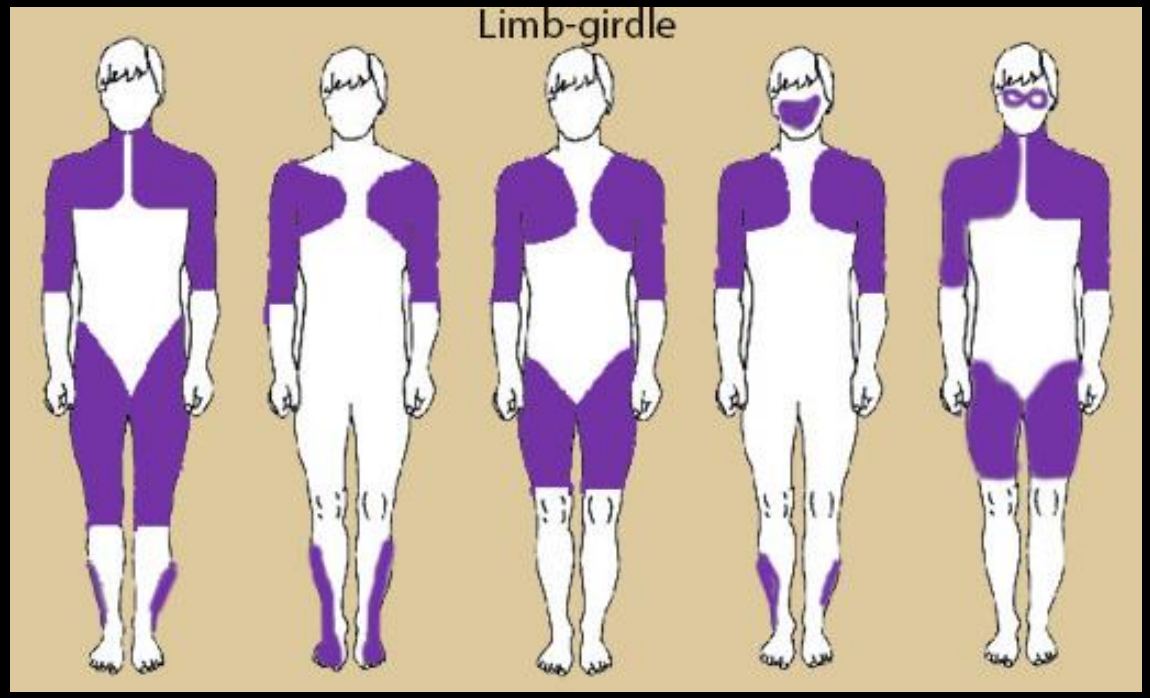
3 mins

Before

After >2mm is +

Myopathy- Weakness

- Usually Painless
  - Unless
    - CTD: dermatomyositis
    - Some toxic- statin
    - Rare metabolic: endocrine, inherited
    - Myotonic dystrophy type 2



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Weakness, but

- Reflexes spared until late
- Normal Sensation
- No Fasciculations
- May have atrophy or hypertrophy

Evaluation for Myopathy

- Creatine kinase, aldolase*
- TFTs, consider other endocrine, systemic
- Consider toxins
- FH
- EMG
- Consult

*elevated with nl CK in some CTD with fascial inflamm

JClin Neuromusc Dis 2002;4:100

Myopathy	Frequency of CK Elevation *	Degree of CK Elevation †
Inflammatory myopathy	3+ to 4+	1+ to 3+
Hypothyroid	3+	1+ to 3+
Other endocrine	0 to 1+	
Chronic *steroid* myopathy	0	
Colchicine, ***Cholesterol drugs***	4+	1+ to 3+
Becker Musc Dystrophy	4+	3+
LGMD	4+	1+ to 3+
Myotonic dystrophy	1+ to 2+	1+
Mitochondrial myopathy	1+ to 2+	1+ to 2+
Glycogen storage	3+	1+ to 2+

* 0=never
1+=<25%
2+=25-50%
3+=51-75%
4+=>75%

† 1+=<4x
2+=4-10x
3+=>10x

Myositis Autoantibody Subsets

Courtesy of Chet Oddis, MD

Anti-synthetases

PL-7

EJ

PL-12

Jo-1

Mi-2

TIF-1γ

DM

Immune-mediated nec myopathy

HMGCR

SRP

SRP

PM

NXP2

Overlap

PM-Scl

U1RNP

Ku

SLE

SSc

Inclusion body myositis

- Proximal weakness
- Distal weakness
- Asymmetry, atrophy
- Dysphagia - 1/3
  - "No" cancers
  - Sjogren Syn, HIV
  - IBM Ab (NT5Cla)-
    50% sens; 92% specific

M>F
>50 yrs

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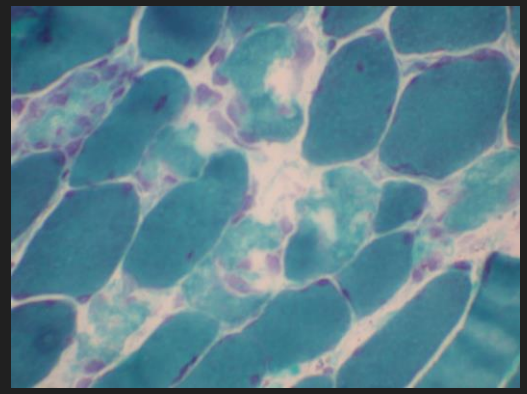
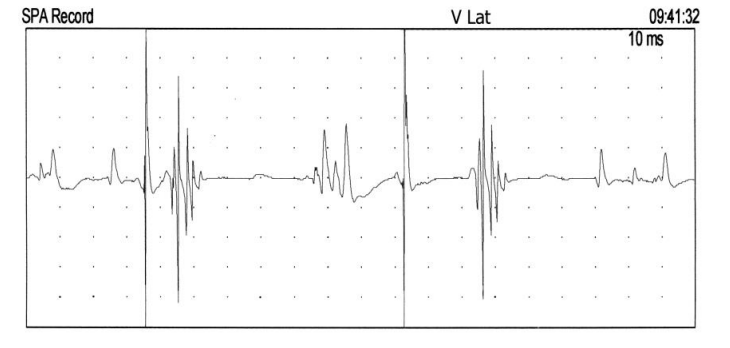
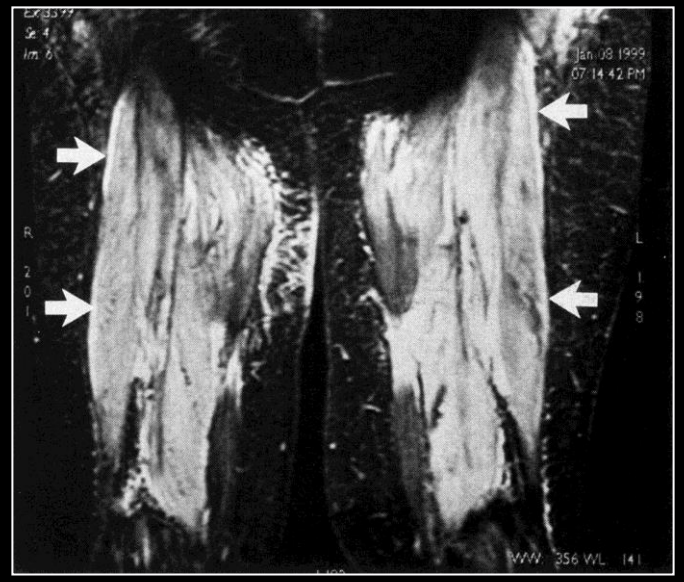
Statin Myopathies

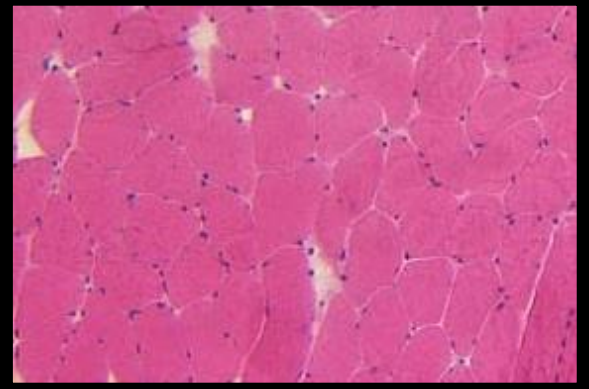


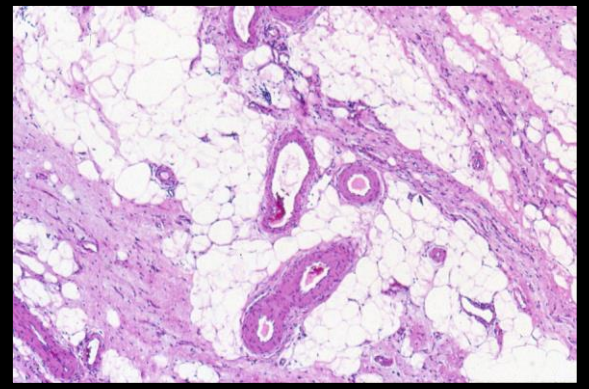
- Mild muscle sxs are cm in statin-treated pts
  - Ideally get a CK before starting statin
- Rhabdomyolysis is rare
- Look for co-morbid factors or polypharmacy in statin patient with myopathic symptoms
- An immune mediated necrotizing myopathy is rare (very *high CK*)
  - Pts don't improve after D/C statin; need immunoRx
  - +HMGCR antibodies
    - Not only seen in statin-exposed pts
    - Not seen with PCSK9 inhibitors

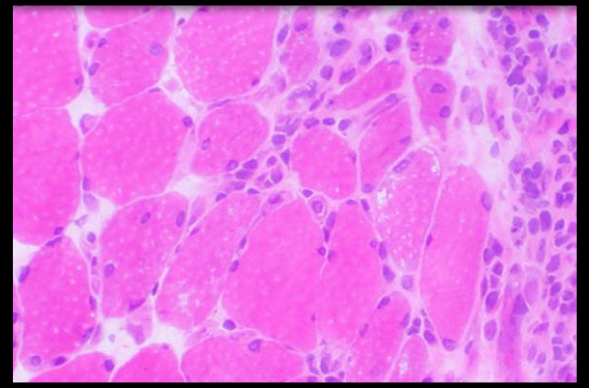
Muscle Biopsy











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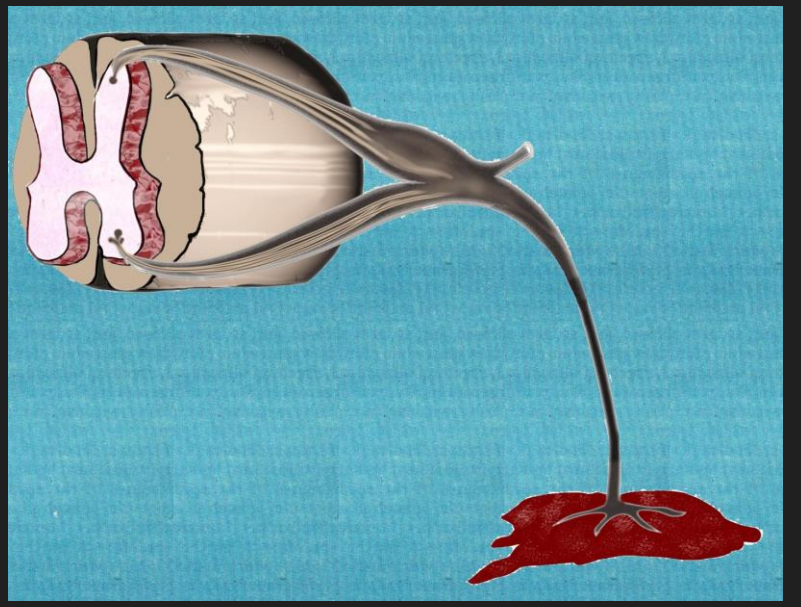
Conclusions

- Overview of Adult Neuromuscular Diseases
  - Approach to Dx
    - Weakness with Patterns
    - Paresthesias
- Diff Diagnoses Based on Localization
  - MND, PN, NMJ, Myopathy
- How to Start the Eval
- When to get Help

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