MYOPATHY, NEUROMUSCULAR JUNCTION & NERVE DISORDERS: Points in differential diagnosis

Distinctive Features: Most myopathies have weakness that is maximal proximally.

Extraocular muscles weak
Myasthenia Gravis (MG)
Thyroid; Botulism; Ocular myositis
Mitochondrial: KS; PEO; MNGIE
Centronuclear; Multicore
Oculopharyngeal MD; IBM + Contracture
Oculopharyngodistal myopathy
Congenital ophthalmoplegias

Periocular without EOM Weakness
Dystrophies: Myotonic;
FSH; Oculopharyngeal
Myasthenia Gravis (MG)
Congenital Myopathies
Rule out: VII nerve lesion

Bulbar dysfunction
MG; Thyroid; Cranial nerve Δ
Oculopharyngeal MD; MG
Distal myopathy (MPD2)
IBM (IM-VAMP); Scleroderma
Motor neuron Δ: ALS; BSMA
Pseudobulbar; Fazio-Londe
Brown-Vialetto-van Laere

Posterior neck weak
Common: MG; PM; ALS
Focal myopathy: Neck; Paraspinous
Rare: FSH dyst; LMN synd; IBM;
Rod; PROMM; Acid maltase; ↓ K^+
Carnitine; Endocrine; Desmin
Camptocormia

Distal & Proximal weakness
Dystrophy: Myotonic; FSH
Scapuloperoneal
Myopathy: Congenital; Distal
Glygogenoses: Debrancher
Phosphorylase b kinase
Neuropathy + Myopathy: Paraneoplastic;
Sarcoid; Mitochondria; HIV;
Drugs (Amiodarone; Doxorubicin
Colchicine; Chloroquine)

Acute weakness
Myasthenia gravis; Myoglobinuria
Myosin loss myopathy; Carnitine ↓
Periodic paralysis: X-Episodic Xp22
Hypo K: CACNA1S; SCN4A; KCNE3
Hyper K: SCN4A; KCNE3
Andersen: KCNJ2
Electrolyte disorders: K ↑ or ↓;
Mg ↑; PO_4 ↓; Barium
Rule out: Neuropathy (GBS);
Spinal cord

Wasting > Weakness (Muscle)
Pathology: Type II atrophy
Sarcopenia; Disuse;
Cachexia: Wt loss > 15%; Age
Paraneoplastic

Weakness > Wasting
Immune myopathy; Myoglobinuria;
Periodic Paralysis;
Myasthenia gravis;
Neuropathy + conduction block

Proximal arms weak
Dystrophy: Scapuloperoneal; FSH
BCIM; Absent muscles; Shoulder joint Δ
MG; Neuropathic: ALS; P-LMN;
Brachial plexopathy

Quadriceps weak
LGD: Becker; 1B; 2B; 2H; Ring fib
Myositis: IBM; Mitochon; Focal
Nerve: Femoral; LS plexopathy;
Diabetic amyotrophy; L3-L4 root

Myoglobinuria
Hereditary: Glycogenolysis; CPT II; LPIN1
Malignant Hyperthermia; Central core
King-Denborough; DMD (Some)
↓ K^+: Licorice; Li; Thiazide;
Amphotericin; Laxative
Infections; Mitochondrial; Trauma
Muscle: Ischemia; Overactivity; PM
Neuroleptic malignant syndrome
Drugs: Heroin; Phencyclidine; e-ACA
Clofibrate + Renal failure;
Cyclosporine A + Lovastatin
Toxins: Venoms; IV drugs
Oral: Haff; Mushrooms; EtOH

Muscle activity
Brody's syndrome: ATP2A1
Cramps: Benign
Myoedema
Myotonia Congenita
Dominant (Thomsen): CLCN1 (Cl)
Recessive (Becker): CLCN1
Acetazolamide responsive: SCNA4
Myotonic Dystrophy 1: DMPK, CTG rpt
Myotonic Dystrophy 2: ZNF9, CCTG rpt
Paramyotonia: Na channel (SCNA4)
Periodic paralysis, Hyperkalemic
Schwartz-Jampel: Perlecan
Neural & Spinal activity

Cardiac disorders
Dystrophy: DMD/Becker;
Myotonic; McLeod;
Emery-Dreifuss; Barth;
Scapuloperoneal; Desmin
Polymyositis; Nemaline rod
Acid Maltase; Debrancher
Carnitine ↓; Desmin ↑
Mitochondrial; Amyloid
Drugs: Metronidazole;
Emetine; Chloroquine;
Clofibrate; Colchicine
Cardiomyopathy + cores
Periodic paralyses

Respiratory Failure
Myasthenia gravis
Myosin-loss myopathy
Acid Maltase
Amyloid; Desmin
Polymyositis (Jo-1)
Congenital Myopathy:
Rod; Centronuclear
Hydroxychloroquine
Neural: Phrenic lesions
Arnold-Chiari; Churg-Strauss
Brachial plexopathy; ALS

GI disorders: See Neuropathy

Muscle pain
Myositis: + Conn tissue dis; Aldolase ↑
Polymyalgia; Rhabdomyolysis
Infections: Trichinosis; Brucellosis
Myoadenylate deaminase ↓ (< 2%)
Myopathy +: Tubular aggregates;
Focal ↓ mitochondria
Drugs: Azathioprine; Steroid ↓...
Rule out:
Small fiber neuropathy; Phlebitis
Bone & joint pain; Muscle Ischemia

Large muscles
Overusage: Myotonia; Exercise
Neural Overactivity
Partial denervation
Endocrine: ↓ Thyroid; Acromegaly
Hered: DMD; LGMD; Lipodyst; Myostatin
Infection: Cysticercosis;
Trichinosis; Schistosomiasis
Drugs: β_2 adrenergic; Androgen
Storage: Glycogen; Amyloid
Fat; Gangliosides
Short stature: Schwartz-Jampel; Myhre

Cramps: Nerve > Muscle
Normal: Single Muscles
Post-contraction; Sleep
Electrolyte: Dehydration
↓ Na, Mg, Ca, Glucose
Endocrine: Thyroid; ↓ Adrenal
Drugs; Pregnant; Spine stenosis
Cramp-fasciculation; Familial
Myopathy: Becker
Motor neuron: ALS
Elecrically silent: phosphorylase
Rippling muscle; Brody's

Contractures
Arthrogryposis
Ullrich/Bethlem: COL6 & 12A1
Congenital MD
Dermatomyositis (DM-VP)
LGMD: Dystrophin; CAPN3
Emery-Dreifuss
IM drug injections
Rigid spine
SMA: SMN; X-linked
Tel Hashomer
Williams-Beuren

CNS + Myopathy
Congenital MD: Santavuori POMGnT1;
Merosin; Fukuyama Fukutin;
Integrin-α7
Dystrophy: DMD; McLeod
DM1; DM2; HIBM
Other hereditary: Mitochondrial
Acid Maltase: Aneurysms
Phosphoglycerate Kinase
Acquired: Myosin-loss; Thyroid
Necrotizing
Encephalopathy; Pipestem capillaries
Hearing loss: FSH; Scapuloperoneal; Mito

Antibodies + Myopathy
MG: Anti-AChR Binding
+ Thymoma: Striation TTN, ACTN, RYR1
LEMS: P-type Calcium channel
Immune myopathies
t-RNA synthetase (Jo-1 + other):
Lung; Raynaud's; Arthritis
Signal recognition Particle: Severe
HMGCR: IMPP + Necrosis
TIF1γ: DM-VP; Neoplasm-associated
DM: Mi-2 Nail Δ; MDA5 Ulcers
NT5C1A: IM-VAMP (sIBM)
PM-Scl: PM + Scleroderma
Decorin: M-protein; Myopathy

CK: High > 1,000
Dystrophy
X-linked: DMD/Becker
Recessive: 2A-2I
Dominant: 1C; Ankle contract
Distal myopathy: Miyoshi
Immune myopathy
SRP, HMGCoAR & Jo-1 Ab;
Paraneoplastic (RIIM); LHIM
Acid maltase
Acute damage: Injection
Rhabdomyolysis; Trauma
Thyroid: Hypo-

Immune & Inflammatory Myopathy
Antibodies: Decorin; SRP; Mi-2;
t-RNA synthetase (Jo-1 75%); HMGCR
Perimysial pathology (IMPP)
Vasculopathy: Dermatomyositis; RIIM
Brachio-cervical inflammatory (BCIM)
Granulomatous ± Sarcoid
Polymyopathy (CK high; No inflammation):
SRP; Paraneoplastic (RIIM); LHIM
IM-VAMP: Inclusion body; PM-Mitochondria
Systemic disease: Drugs; GVHD
Collagen vascular; Infection;
Malignancy; Toxic
Hereditary: FSH

Myasthenic Syndromes

Acquired MG: Immune ± Thyroid or Thymoma;
Childhood; Drug-induced; Neonatal Transient
Lambert-Eaton myasthenic syndrome (LEMS)
Congenital & Familial:
Presynaptic: Familial infantile (ChAT)
↓ Synaptic vesicles & Quantal release
Congenital Lambert-Eaton-like; SLC18A3
Episodic ataxia 2: CACNA1A; SLC5A7
Synaptic: AChE deficiency (ColQ)
Postsynaptic: AChR α β δ e; Rapsyn; Plectin
AChRs: Kinetic Δ & ↓ # @ NMJs
Slow AChR channel; ↓ Channel open time
AChRs: Kinetic Δ & Normal # @ NMJs
↑ Conductance & Fast closure of AChRs
↓ ACh-affinity & Fast-channel
AChRs: ↓ #s @ NMJs & Kinetic WNL
Rapsyn: ↓ AChRs @ NMJs
Plectin; MuSK; Dok-7; LRP4; SNAP25
SCN4A (Apnea & Bulbar);
Limb-girdle MG: GFPT1; DPAGT1; ALG2; RYR1
Other: Agrin; ALG14; SCN4A; ZC4H2; CNTN1
TPM3; Congenital LEMS-like; COL13A1
Familial immune; PREPL

Hereditary Myopathy Syndromes

Dystrophies: Limb-Girdle & Other
Dominant: 1A MYOT; 1B LMNA; 1C Cav3 (AD & AR);
1D DNAJB6; 1E DES; 1F TNPO3; 1G 4p21; 1H 3p23
Cytoplasmic body MYH7, Titin; Bethlem COL6A1,2,3
Emery-Dreifuss LMNA, SYNE 1&2; Hyaline body MYH7
Myotonic dyst: 1 DMPK CTG rpt; 2 ZNF9 CCTG rpt
IBM: 1 Desmin; 3 Myosin HC2; Paget VCP
FSH DUX4 del;. Oculopharyngeal PABP2 GCG rpt;
Myofibrillar: Desmin; αB-crystallin; BAG3; ACTA1
ZASP; Myotilin; FLNC; SEPN1; RBCK1; TPM2; TPM3
Dysplasia Diaphys TGFB1; Epiphys COL9A 2& 3, COMP
Recessive: 2A Calpain-3; 2B DYSF; 2G TCAP; 2H TRIM32;
Sarcoglycan 2C γ; 2D α; 2E β; 2F δ; 2I FKRP; 2J Titin;
2K POMT1; 2L; 2M FKTN; 2N POMT2; 2O POMGnT1;
2P DAG1; 2Q Plectin; 2R Desmin; 2S TRAPPC11; 2T GMPPB
2U ISPD; 2V GAA; 2W LIM2; 2X POPDC1; 2Y TOR1AIP1
2Z POGLUT1; COL6A2; MYH2
DPM2 (Epilepsy); DPM3 (Cardiomyopathy); PTRF; POMGNT2
CMD: FKRP; SEPN1; POMT1;; POMT2; FKTN; LARGE;
GTDC2; TMEM5; B3GALNT2; SGK196; B3GNT1; GMPPB
ISPD; Resp fail 1q42; Ullrich COL6A; Laminin α-2
X-linked: Barth Tafazzin; Autophagy VMA21; XMEA VMA21
Emery-Dreifuss Emerin; Danon LAMP-2; McLeod XK;
Becker & Duchenne Dystrophin; Scapuloperoneal FHL1

Distal Myopathies
Dominant:
Welander TIA1: Late; Hands & Ant. Legs
Finnish Titin: Late; Ant Tib
Gowers-Laing (MPD1) MYH7: Adult; Ant leg
Dystrophy + Rimmed vacuoles
IBM1 (Quad) Desmin; MPD2 (Vocal cord) MATR3
MPD3: Adult, Asymmetric; LGD 1A & 1C
IBM +: Paget VCP; HNRNPA2B1; HNRNPA1
Oculopharyngodistal; Scapuloperoneal
Myofibrillar
Recessive:
Nonaka & IBM2 GNE: Quad sparing
Miyoshi & LGD 2B DYSF: Early adult; Post leg
MMD3 ANO5: Post leg
LGD 2G Telethonin: Teens; Ant leg & Prox

Congenital myopathy Core RYR1; Rod;
Centronuclear; Spindle excess HRAS
Other myopathies
Barnes; Congenital; Lipid; Glycogen;
Familial MG; Tubular Aggregates