

MYOPATHY, NEUROMUSCULAR JUNCTION & NERVE DISORDERS: Points in differential diagnosis			
1. Distinctive Features: Most myopathies have weakness that is maximal proximally.			
<p>Extraocular muscles weak Myasthenia Gravis (MG) Thyroid; Botulism Mitochondrial: KS; PEO; MNGIE Centronuclear; Multicore Oculopharyngeal MD; IBM + Contracture Oculopharyngodistal myopathy Congenital ophthalmoplegias</p>	<p>Periocular without EOM Weakness Dystrophies: Myotonic; FSH; Oculopharyngeal Myasthenia Gravis (MG) Congenital Myopathies Polymyositis Rule out: VII nerve lesion</p>	<p>Bulbar dysfunction MG; Thyroid; Cranial nerve Δ Oculopharyngeal MD Distal myopathy (MPD2) Polymyositis: IBM; Scleroderma Motor neuron Δ: ALS; BSMA Pseudobulbar; Fazio-Londe Brown-Vialetto-van Laere</p>	<p>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</p>
<p>Distal & Proximal weakness Dystrophy: Myotonic; FSH Scapuloperoneal Myopathy: Congenital; Distal Glycogenoses: Debrancher Phosphorylase b kinase Neuropathy + Myopathy: Paraneoplastic; Sarcoid; Mitochondria; HIV; Drugs (Amiodarone; Doxorubicin Colchicine; Chloroquine)</p>	<p>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 ↑; PO₄ ↓; Barium Rule out: Neuropathy; Spinal cord</p>	<p>Wasting > Weakness Pathology: Type II atrophy Cachexia: Wt loss > 15% Disuse; Steroid myopathy; Paraneoplastic; Aging</p>	<p>Proximal arms weak Dystrophy: Scapuloperoneal; FSH Absent muscles; Shoulder joint Δ MG; Neuropathic: ALS; P-LMN; Brachial plexopathy</p>
<p>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; ε-ACA Clofibrate + Renal failure; Cyclosporine A + Lovastatin Toxins: Venoms; IV drugs Oral: Haff; Mushrooms; EtOH</p>	<p>Muscle activity Brody's syndrome: ATP2A1 Cramps: Benign Myoedema Myotonia Congenita Dominant (Thomsen): CLCN1 (Cl⁻) Recessive (Becker): CLCN1 Acetazolamide responsive: SCN4A Myotonic Dystrophy 1: DMPK, CTG rep Myotonic Dystrophy 2: ZNF9, CTTG rep Paramyotonia: Na⁺ channel (SCNA4) Periodic paralysis, Hyperkalemic Schwartz-Jampel: Perlecan Neural & Spinal activity</p>	<p>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</p>	<p>Respiratory Failure Myasthenia gravis Myosin-loss myopathy Acid Maltase Amyloid; Desmin Polymyositis; Nemaline rod Congenital Myopathy: Rod; Centronuclear Hydroxychloroquine Neural: Phrenic lesions Arnold-Chiari; Churg-Strauss Brachial plexopathy; ALS</p>
<p>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</p>	<p>Large muscles Overusage: Myotonia; Exercise Neural Overactivity Partial denervation Endocrine: ↓ Thyroid; Acromegaly Hered: DMD; LGMD; Lipodyst; Myostatin Infection: Cysticercosis; Trichinosis; Schistosomiasis Drugs: β₂ adrenergic; Androgen Storage: Glycogen; Amyloid Fat; Gangliosides Short stature: Schwartz-Jampel; Myhre</p>	<p>Cramps 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 Electrically silent: phosphorylase Rippling muscle; Brody's</p>	<p>Contractures Arthrogyposis Bethlem Myopathy Congenital MD Dermatomyositis Dystrophinopathies Emery-Dreifuss IM drug injections Rigid spine syndrome SMA: 5q; X-linked Tel Hashomer Williams-Beuren</p>
<p>CNS + Myopathy Congenital MD: Santavuori POMGnT1 1p32; Merosin 6q22; Fukuyama Fukutin; 9q31 Integrin-α7 12q13 Dystrophy: DMD; McLeod DM1; PROMM; HIBM 9p13 Other hereditary: Mitochondrial Acid Maltase: Aneurysms Phosphoglycerate Kinase Acquired: Myosin-loss; Thyroid Necrotizing Encephalopathy; Pipestem capillaries Hearing loss: FSH; Scapuloperoneal; Mito</p>	<p>Antibodies + Myopathy MG: Anti-AChR Binding & Modulating MG + Thymoma: Anti-striational vs. Titin; Actinin; Ryanodine Recept LEMS: P-type Ca⁺⁺ channel Immune myopathies t-RNA synthetase (Jo-1 + other): Lung; Raynaud's; Arthritis Signal recognition Particle: Acute; Severe Mi-2: Dermatomyositis; Nail Δ PM-Sc: PM + Scleroderma Decorin: M-protein; Myopathy</p>	<p>CK: High > 1,000 Dystrophy X-linked: DMD/Becker Recessive: 2A-2l Dominant: 1C; Ankle contract Distal myopathy: Miyoshi Polymyositis Acid maltase Acute damage: Injection Rhabdomyolysis; Trauma Thyroid: Hypo-</p>	<p>Inflammatory myopathies Antibodies: Decorin; SRP; Mi-2; t-RNA synthetase (Jo-1 75%) Dermatomyositis: Child; Mi-2; Adult Microvasculopathies: DM; SRP Brachio-cervical inflammatory (BCIM) Granulomatous ± Sarcoid Idiopathic myositis: Poly-; Focal Inclusion body (IBM); PM-Mitochondrial Systemic disease: Drugs; GVHD Collagen vascular; Infection; Malignancy; Toxic Hereditary: FSH</p>
2. Myasthenic Syndromes		3. Hereditary Myopathy Syndromes	
<p>Acquired MG: Immune ± Thyroid or Thymoma; Childhood; Drug-induced; Neonatal Transient Lambert-Eaton myasthenic syndrome (LEMS) Congenital & Familial: Presynaptic: Familial infantile (ChAT; 10q11) ↓ Synaptic vesicles & Quantal release Congenital Lambert-Eaton-like Episodic ataxia 2: CACNA1A; 19p13 Synaptic: AChE deficiency (CoIQ; 3p25) Postsynaptic: AChR α β δ ε; 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 (11p11); ↓ AChRs @ NMJs Plectin 8q24; MuSK 9q31; Dok-7 4 Apnea & Bulbar: SCN4A 17q35 Other syndromes: Familial limb-girdle; Benign congenital MG & Facial malform Congenital LEMS-like; Familial immune</p>	<p>Dystrophies: Limb-Girdle & Other Dominant: 1A Myotilin (TT1D), 5q31; 1B LMNA, 1q11; 1C Cav-3, 3p25; 1D 7q; 1E 6q23; 1F 7q32; 1G 4p21; Cytoplasmic body 2q24 & 2q21; Bethlem COL6A, 21q22, 2q37 Emery-Dreifuss LMNA, SYNE 1&2; Hyaline body MYH7 14q12 Myotonic dyst: 1 DMPK CTG rpt, 19q13; 2 ZNF9, 3q21 IBM: 1 Desmin; 3 Myosin HC2, 17p13; Paget VCP, 9p13 FSH 4q35; Oculopharyngeal PABP2 GCG rpt, 14q11; Myofibrillar: Desmin 2q35; αB-crystallin 11q22; BAG3 10q25 ZASP, 10q22; Myotilin; FLNC 7q32; SEP1 1p36 Dysplasia Diaphys TGFB1, 19q13; Epiphys COL9A3, 20q13 Recessive: 2A Calpain-3, 15q15; 2B Dysferlin, 2p12; Cav-3; Sarcoglycan 2C γ, 13q12; 2D α, 17q21; 2E β, 4q12; 2F δ, 5q33 2G Telethonin, 17q11; 2H TRIM32, 9q31; 2I FKR, 19q13; 2J Titin, 2q31; 2K POMT1, 9q34; 2L, 11p13; 2M Fukutin, 9q31; 2N POMT2 14q24; COL6A2; 21q22 CMD: NI CNS FKR, 19q13; Rigid spine SEP1, 1p35 Resp fail 1q42; Ullrich COL6A; Laminin α-2 6q22 X-linked: Barth Tafazzin, Xp28; Autophagy Xq28; Emery-Dreifuss Emerin, Xq28; Danon LAMP-2 Xq24 Becker & Duchenne Dystrophin; Xq21; XMEA VMA21 Xq28 McLeod XK Xp21; Scapuloperoneal FHL1 Xq26</p>	<p>Distal Myopathies Dominant: Welander 2p13: Late; Hands & Ant. Legs Finnish Titin, 2q31: Late; Ant Tib Gowers-Laing (MPD1) MYH7, 14q11: Adult; Ant leg Dystrophy + Rimmed vacuoles 19p13 IBM1 (Quad weak) Desmin MPD3: Adult, Asymmetric; LGD 1A & 1C IBM +: Page's VCP, 9p13; Resp failure 6q27 Oculopharyngodistal; Scapuloperoneal 12q13 Vocal cord & Pharyngeal (MPD2) 5q31 Myofibrillar: Desmin; αB-crystallin; TT1D; ZASP SEP1; Filamin C; BAG3 Recessive: Nonaka & IBM2 GNE, 9p12: Quad sparing Miyoshi & LGD 2B Dysferlin, 2p12-14 Early adult; Posterior leg LGD 2G Telethonin, 17q11: Teens; Ant leg & Prox</p>	
		Other myopathies Barnes; Congenital; Lipid; Glycogen; Familial MG; Tubular Aggregates	