Myalgia

- **Polymyaglia Rheumatica (PR)**
  - Epidemiology
    - elderly female
  - S/S
    - abrupt onset, proximal bilateral muscle pain and stiffness (>2/3 of the following areas: torso/neck, shoulder/prox arm, or hips/prox legs) after inactivity but NO weakness, that is self-limited lasting ~1-2yrs,
    - depression very common
    - DOE
    - 10% have temporal arteritis and 50% of pts with temporal arteritis have PR
  - Labs
    - increased APRs
  - Tx
    - low dose steroids which you begin tapering after 4-6wks with complete cessation after 2yrs
- **Fibromyalgia**
  - Epidemiology
    - Adult female
    - 2% of the population
    - RFs: + FHx, psyh dz, low education, low income
  - Mechanism
    - Unknown but some believe that there is pain amplification 2/2 changes in CNS [NT]
  - S/S & Dx
    - DOE (esp no depression, sleep disturbance, rhuem esp PMR/SLE/RA, hypoTH, etc)
    - Nonprogressive but waxes/wanes, chronic (>3mo) trigger (~4kg of force) points (must have R/L and upper/lower ad axial triggers w/ ≥11/18: occiput, anterior neck, upper border of trapezius, above medial scapula spine, 2nd rib lateral to costochondral jxn, 2cm distal to lateral epicondyle, upper outer buttock, trochanter, medial knee proximal to joint)
    - Other S/S: pt not only complain of muscle pain but also stiffness, body aches, fatigue, disrupted sleep pattern, anxiety, depression that is aggravated by change in weather, stress, sleep deprivation, stress , overactivity or prolonged inactivity, etc
    - NB there are NO microscopic or biochemical abnormalities
    - NB pts often have concurrent IBS, migraines, chronic fatigue syndrome (CFS), temporomandibular joint pain, MDD
    - NB pts often have a precipitating physical/psychologic event
  - Tx (address comorbidities)
    - Med Tx
      - 1° Elavil, Flexeril
      - 2° Ultram, SSRIs, SNRIs, Lyrica
      - NO Evidence: Opioids, NSAIDs, Benzo, Steroids
    - Non-Med Tx
      - 1° pt education (reassurance that the pt's Sx are real but non-life threatening/progressive/non-deforming, advise pts to avoid harmful/expensive Tx, help pts manage the social/financial aspects of their life), CV exercise, CBT
      - 2° accupuncture, strength exercise, hypnotherapy, good sleep hygiene
      - NO Evidence: trigger point injections, flexibility exercise like yoga, chiropractor, massage, ultrasonography, electrotherapy

Myositis

- **Polymyositis (PM)**
  - Epidemiology
    - Two Peak Ages: ~15yo and ~45yo
    - AA>White, F>M
  - S/S
    - Gradual Onset (over months) Progressive Symmetric Proximal Weakness
      - Because proximal ask about specific activities like rising from a chair, climbing stairs, hair combing, reaching for objects high on shelves, etc
      - Occasional myalgia and TTP but very mild unlike polymyalgia rheumatic and fibromyalgia
      - Atrophy is seen only in long-standing untreated cases
    - Other Affected Systems (always check for weight loss b/c it is a marker for GI involvement (poor prognostic indicator) and cancer (obviously poor prognostic indicator)
      - General: Constitutional Symptoms
      - Vessels: Vasculitis, Raynaud's, Anti-Phospholipid Syndrome
      - Joint: Arthralgia/Arthritis (small symmetric joints of the hand) worse if +anti-Jo-1
      - GI: Pharyngeal/Esophageal Muscle Weakness resulting in dysphagia, regurgitation, aspiration, hoarseness (*high mortality*), many other GI problems

- Pulm: Chronic Interstitial Lung Disease (*very common, under-recognized, and high morbidity*), Acute Alveolitis, Respiratory Muscle Weakness but rarely respiratory failure (*high mortality*), Aspiration Pneumonitis/Pneumonia, PCP 2/2 steroids
- Cardiac: Myocarditis leading to effusions, CHF, fibrosis, etc and Conduction Abnormalities but most pts rarely have dangerous arrhythmias (*high mortality*) most just have asymptomatic nonspecific changes

▪ Higher Risk (2x) of Malignancy
- Association first established in 1916 (Stertz G. Polymyositis. Berl Klin Wochenschr. 1916;53:489.)
- Risk is highest at time of diagnosis and up to 5yrs thereafter then risk decreases
- RFs: older age, male, more rapid, severe skin/muscle dz, higher APR, lower complement, antibody (+anti-p155/140, one study reported +Ab in 79% of DM pts w/ malignancy vs 11% of DM w/o malignancy)
- Incidence: 24% (DM) vs 10% (PM)
- Pathogenesis: immune reaction to the tumor cross-reacts w/ antigens (Mi-2 and Jo-1) in skin/muscle
- Types of malignancies correlate with those that develop in an age-matched population (except with *ovarian* cancer which is increased in atypical age groups) and they include usually cancer of visceral organs esp ovary (RR 10.5, 95% CI 6.1-18.1), lung (5.9, 95% CI 3.7-9.2), pancreatic (3.8, 95% CI 1.6-9.0), stomach (3.5, 95% CI 1.7-7.3), colorectal (2.5, 95% CI 1.4-4.4), NHL (3.6, 95% CI 1.2-11.1)
  - NB in the Asia/Africa the most common malignancy is nasopharyngeal carcinoma
- Currently, no guideline exists for screening pts but some actions are commonly taken
  - aggressively look for cancer during the first few years (b/c most present around the time of diagnosis of PM/DM) w/ PEx, tumor markers, imaging thereafter investigate when symptoms concerning for cancer arise or when there is a relapse in myositis because it often can herald a new cancer
  - Exception: for ovarian cancer which is common and can occur at atypical ages it is recommend that women get regular CT of the pelvis and CA-125
- DM/PM improves after successful Tx of malignancy
- DM/PM worsens with tumor recurrence

▪ Anti-Synthetase Syndrome
- Seen in 30% of PM/DM
- Acute onset of Constitutional Symptoms, Myositis, Raynaud's, Mechanic's Hands, Poly-arthritis, ILD
- + Anti-Synthetase Abs

▪ IIM can be associated with other rheumatologic diseases (MCTD) and some rheumatologic diseases can have myositis as a symptom but do not fill the criteria for a IIM

o Dx

▪ Bohan and Peter Criteria (NEJM 1975;292:344)
- Symmetrical Weakness
- Elevated Muscle Enzymes
- Positive Biopsy
- Positive EMG
- ± Cutaneous Changes (for DM)
- NB does not take into account auto-antibodies and does not recognize IBM therefore new classification schemas are being established which include clinical, histopathologic, laboratory, and autoantibody findings
- NB "Possible" if 2 symptoms, "Probable" if 3 symptoms, "Definite" if 4 symptoms
- NB Amyopathic DM aka DM Sine Myositis (no muscle findings but cutaneous findings for >2yrs)

▪ Abnormal Electromyography (EMG)
- Sensitivity (85%) Specificity (low)
- Triad of Increased Membrane Irritability
  - Spontaneous Fibrillations
  - Repetitive High Frequency Discharges
  - Low Amplitude, Shorter Duration, Polyphasic Potentials
- Always perform last because the process can damage muscle and elevate enzymes on lab and elicit inflammation seen on MRI
- Helps in distinguishing myopathic weakness from neuropathic weakness

▪ Muscle Biopsy (critical for dx)
- Sensitivity (80%) Specificity (90%)
- MRI muscle to locate inflammation for biopsy (usually muscles are the quadricep/deltoid/neck) if you use EMG go to exact contralateral side to dx symmetric weakness (one side EMG the other Bx)
- General: muscle fiber degeneration and regeneration, necrosis, phagocytosis
- PM Specific Bx: CD8 T-Cell Lymphocytic infiltrate *within* muscle fascicles w/ affected fibers throughout the fascicle
- NB Biopsy is able to differentiate the three different primary myositis

- NB Always perform last because the process can damage muscle and elevate enzymes on lab and elicit inflammation seen on MRI

- MRI
  - Sensitivity (90%) Specificity (low)
  - Can show inflammation (active dz) on T2 weighted images and atrophy and fatty infiltration (inactive dz) on T1 weighted images
  - NB b/c non-invasive it can be used to serially assess response to therapy
- Lab
  - Elevated Muscle Enzymes
    - Creatine Kinase (CK) Sensitivity (85%) Specificity (poor)
    - ASpartate aminoTransferase (AST)
    - ALalanine aminoTransferase (ALT)
    - Lactate Dehydrogenase (LDH)
    - Aldolase
    - NB enzyme levels are not proportional to severity of muscle weakness, typically levels lag behind clinical improvement but may be a harbinger for future flares
  - Elevated APRs
  - + Auto-Antibodies
    - Anti-Nuclear Antibodies (ANA)
      - Sensitivity (80%) Specificity (10%)
      - If + look for specific ANAs b/c often there is overlap with other connective tissue diseases
    - Myositis Specific Auto-antibodies (MSAs) (Variable Sensitivity with 90% Specificity)
      - Anti RNA Synthetases
        - 1° Jo-1 (20%) 2° PL-7 (3%), PL-12 (3%), EJ (1%), OJ (1%), KS (1%)
        - Cytoplasmic Antibody
      - Anti Signal Recognition Particle (Anti-SRP) (5%)
        - Cytoplasmic Antibody
        - Associated w/ PM, very high enzyme levels, heart very much involved, acute onset, treatment resistant
      - Anti Nuclear Helicase (Anti-Mi-2) (5%)
        - Nuclear Antibody
        - Associated w/ DM, rash is much more severe but good response to Tx
    - Myositis Associated Auto-antibodies (MAAs)
      - Anti-UI-RNP (seen in MCTD)
      - Anti-PM-SCl (seen in "Overlap Syndrome" of Scleroderma)
      - Anti DNA Mismatch Repair Enzyme (Anti-hPMS-1)
      - Anti Cell Adhesion Molecules (Anti-CDAM-140)

- Treatment
  - Indicators for Poor Prognosis: delayed treatment for >6mo after onset of symptoms, profound weakness, dysphagia, respiratory muscle weakness, ILD, cancer, heart involvement NOT enzyme level
  - Basic Treatment Strategy: systemic enteral high dose steroids for a few months to control disease (if no clinical improvement at this time then add immunosuppressants) follow by a taper over the course of 1yr until you reach the lowest effective dose, most pts then stop steroids and continue immunosuppressant tapering over 6mo
    - The longer the period between onset of symptoms and initiation of treatment the worse the response to steroids
    - 80% of pts improve with steroids alone
    - If continued or worsening muscle weakness despite normalization of enzymes while on steroids consider steroid induced myopathy, IBM, or another diagnosis
    - Some initially start immunosuppressants so that the lowest steroid dose is used to diminish steroid induced myopathy
    - Immunosuppressants: 1° Methotrexate or Azathioprine 2° Cyclosporine, Tacrolimus, IVIG, et al
    - Especially slow tapers are important b/c fast tapers can cause a flare in muscle inflammation
    - Treatment is guided NOT by [enzyme] but by pt's subjective report of weakness and objective physical exam findings on quadracep/deltoid/neck function
  - Adjuvant Therapy
    - PT/OT
    - Aspiration Precautions (HOB Elevated, Thick Diets, etc)
    - Cancer Precautions (Avoid UV Light, etc)
    - Osteoporosis Prophylaxis (Bisphosphanates, Calcium + VitD Supplementation)
    - Infection Prophylaxis (Bactrim for PCP)
  - Routinely Monitor
    - PFTs

        - S/S of Cancer
    - Overall Prognosis
        - only 25% achieve remission, 35% progressive, 20% relapsing/remitting
        - 85% 10yr survival
        - Poor Prognostic Indicators: Increased Age, Delay in Initiation of Tx, Pharyngeal/Esophageal Weakness, ILD, Arrhythmias
- **Dermatomyositis (DM)** (noted differences from PM)
    - Additional Cutaneous Findings
        - Head
            - **Heliotrope Rash** (50%)– lilac rash with occasional edema on upper eyelids
            - **Erythroderma** (uncommon) – erythema around malar region and forehead
            - **Scalp Psoriasis/Pruritus** (uncommon)
        - Trunk
            - **Shawl Sign** (uncommon) – erythema around upper back and shoulders
            - **V Sign** (uncommon)- erythema around upper chest
            - **Flagellate Erythema** (rare), **Panniculitis** (rare), **Vitiligo** (rare), **Cutaneous Mucinosis** (rare), **Multifocal Lipatrophy** (rare), **Poikiloderma** (rare), **Bullous Pemphigoid** (rare), **Icthyosis** (rare)
        - Extremities
            - **Gottron's Papules** (70%) – violaceous plaques with occasional scaling over extensor surfaces of 1° MCP and 2° PIP/DIP 3° Wrist, Elbow, Knee, sometimes mimicking psoriasis
            - **Gottron's Sign** (70%) – erythema in same distribution (but usually 3° locations) but no papules
            - **Periungual Abnormalities** (uncommon) – cuticle hypertrophy, erythema, proximal nail telengectasia, infarcts, et al
            - **Mechanic's Hands** (rare) – rough, scaly, fissured surfaces on the lateral/palmar surface of fingers, also hyperpigmentation of palmar creases looking like trapped grease
            - **Calcinosis Cutis** (rare) – deposition of calcium at sites of trauma leading to ulceration
    - Much Higher Risk (6x) of Malignancy
    - DM Specific Bx: CD4 B-Cell Lymphocytic infiltrate w/ IC Deposition esp the C5b-9 MAC *around* muscle fascicles especially peri/intravascularly w/ affected fibers grouped in one portion of the fascicle
    - Skin Bx: similar histology but it occurs at the dermal-epidermal junction especially peri/intravascularly
- **Inclusion Body Myositis (IBM)** (noted differences from PM)
    - M>F
    - >50yo
    - Insidious (over many years, often diagnosed as treatment resistant PM) Asymmetric Proximal (Early) / Distal (Late) Weakness
    - Less likely to have positive auto-antibodies
    - Lower muscle enzyme levels
    - EMG: mixed myopathic and neuropathic features
    - IBM Specific Biopsy: just like PM but also Amyloid Deposits in Rimmed Vacuoles in Cytoplasm and Tubofilamentous Inclusions ("Inclusion Bodies") in Cytoplasm/Nucleus
    - MRI: more fatty infiltration and muscle atrophy
    - Less responsive to PM/DM treatments
    - Worse prognosis
- **Eosinophilic Myositis, Oribital Myositis, Focal Myositis, Myositis Ossificans**