

# Fibromyalgia for Primary Care Providers

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# Disclosure

- I have no relevant relationships with ineligible companies to disclose within the past 24 months. (Note: Ineligible companies are defined as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.)
- My presentation will talk about the following medications that are used for indications that are not FDA-approved (off-label use)
  - Amitriptyline, despiramine, venlafaxine, reboxetine, esreboxetine, gabapentin, cyclobenzaprine, tizanidine, baclofen, naltrexone, memantine, ketamine, tramadol, quetiapine, and pramipexole for fibromyalgia

# Learning Objectives

- At the conclusion of this session, participants should be able to:
  - Discuss pathophysiology of fibromyalgia
  - Identify triggers and comorbid conditions associated with fibromyalgia
  - Diagnose fibromyalgia utilizing current ACR and/or AAPT criteria
  - Formulate individualized treatment plans for patients with fibromyalgia using holistic approach
  - Utilize appropriate pharmacotherapy for patients with fibromyalgia

# Pre-test Question #1

- Which of the following neurological symptoms is characteristic of fibromyalgia?
  - Apraxia
  - Aphasia
  - Allodynia
  - Ataxia

# Pre-test Question #2

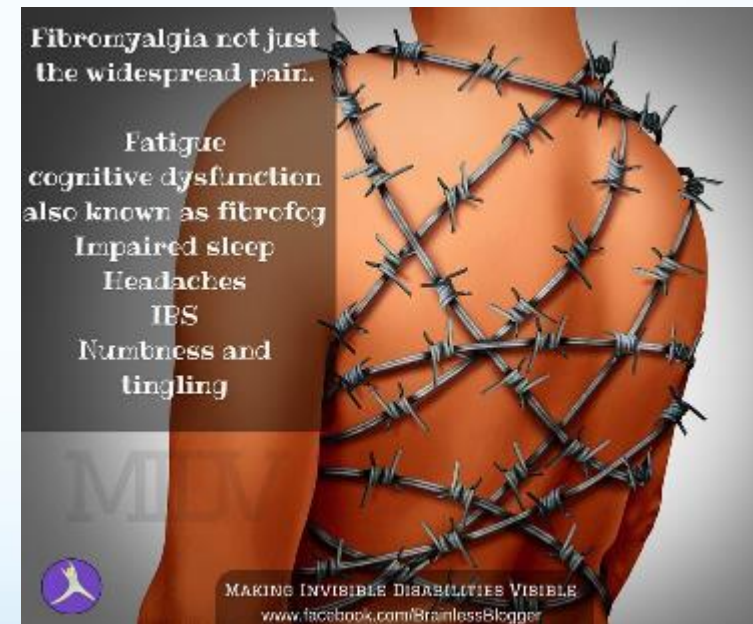
- Which of the following is a first line treatment of fibromyalgia?
  - Exercise program
  - Low-dose opioids
  - Pregabalin
  - Acupuncture

# Pre-test Question #3

- Which of the following is an FDA approved medication for the treatment of fibromyalgia?
  - Fluoxetine
  - Duloxetine
  - Paroxetine
  - Sertraline

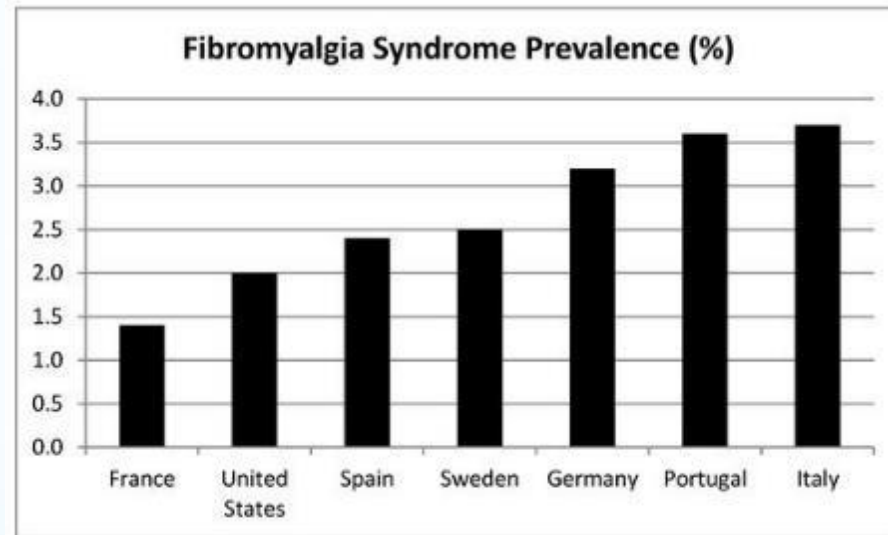
# Fibromyalgia Syndrome

- Chronic widespread pain disorder
  - Aberrant central pain processing and central sensitization
- Migrating and multisite musculoskeletal pain
  - No evidence of inflammation
- Somatic complaints
  - Fatigue and sleep disturbances
  - Cognitive and psychiatric disturbances
- Variable severity and outcomes → large spectrum



# Epidemiology

- Prevalence 2-4%, increases with age
  - Can happen in childhood/adolescence and persist into adulthood
- 2:1 female predominance
  - Most common cause of generalized musculoskeletal pain in women 20-55 years old



*J. Clin. Med.* 2020, 9(4), 1219.



# Epidemiology

- Up to 30% of patients with inflammatory conditions have FMS
  - SLE, RA, etc.
- Up to 65% of patients with FMS have mental health diagnosis
  - Anxiety, depression, etc.
  - Much higher than general population
- Commonly happens in people with other chronic pain syndromes
  - TMJD, chronic back pain, IBS, etc.

# Epidemiology

- Up to 30% of patients with FMS report that they are work disabled
  - Worse outcomes: low SES, obesity, comorbid mental illness, history of abuse, catastrophizing, and excess somatic concern
- More severe symptoms and more comorbidities = higher cost of care and greater morbidity
  - Many rate health as fair/poor
  - Average 1 outpatient visit/month!
  - Spend 3x more on healthcare
- Mortality rates not necessarily increased, but increased risk of suicide
  - More CVD and cancer (due to obesity and/or inactivity?)

# Can't I just send them to rheum?!

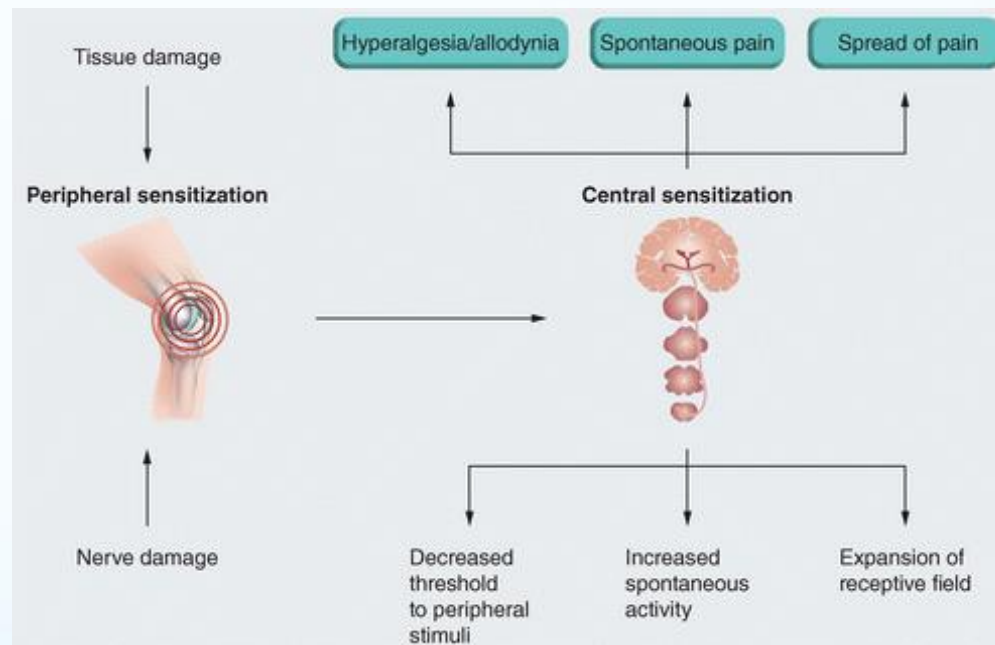
- Rheumatologists are not always necessary
- PCPs can coordinate all aspects of care
  - Comprehensive management with medical home model
  - PCPs have better patient outcomes than tertiary referral centers!
- Continuous management: easier and closer follow up
- Reduced healthcare costs
  - 2+ years to get diagnosed with >3 different consults!

# Pathophysiology of FMS

- Pathophysiology is complex and not quite understood
  - Likely genetic predisposition with environmental triggers
    - 50% concordance rates in similar chronic pain syndromes
  - Possible epigenetic contributions?
  - Etiology unknown but maybe autoimmune connection
- Strong genetic association
  - First degree relatives 8x more likely to have FMS
  - Multiple candidate genes in serotonin, dopamine, and catecholamine metabolic or signaling pathways
    - Not always consistent results with SNPs

# Pathophysiology of FMS

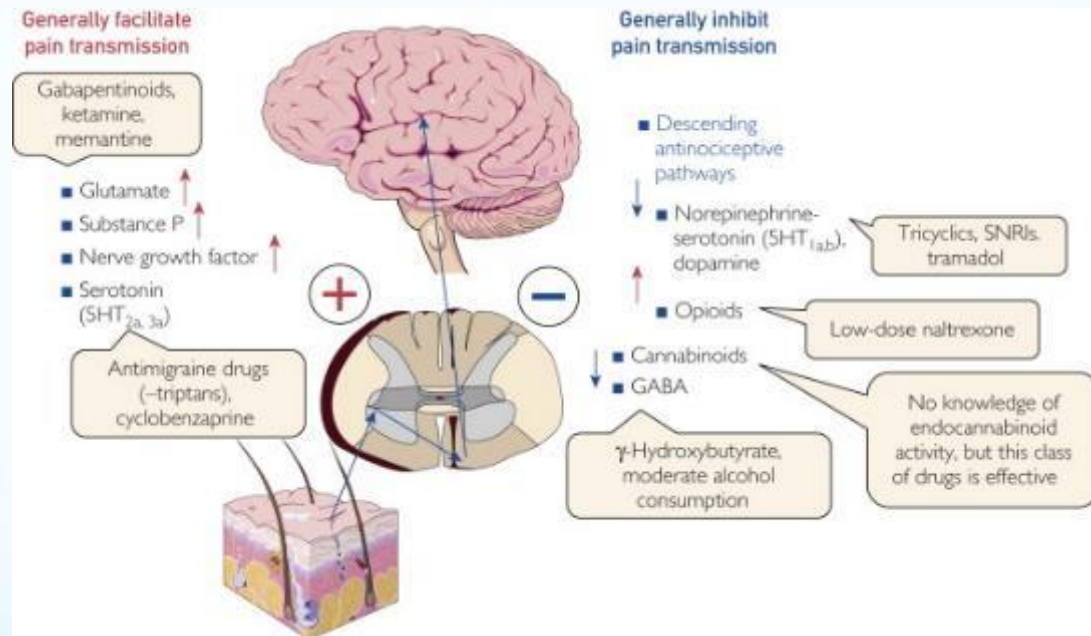
- Dysfunction of CNS pain processing
  - Hyperalgesia: feel more pain than normal
  - Allodynia: feel non-painful as painful
  - Via central sensitization and augmentation
    - Heat, cold, auditory, electrical stimuli



*Future Medicine* 2014 14-37. <https://doi.org/10.2217/fmeb2013.13.160>

# Pathophysiology of FMS

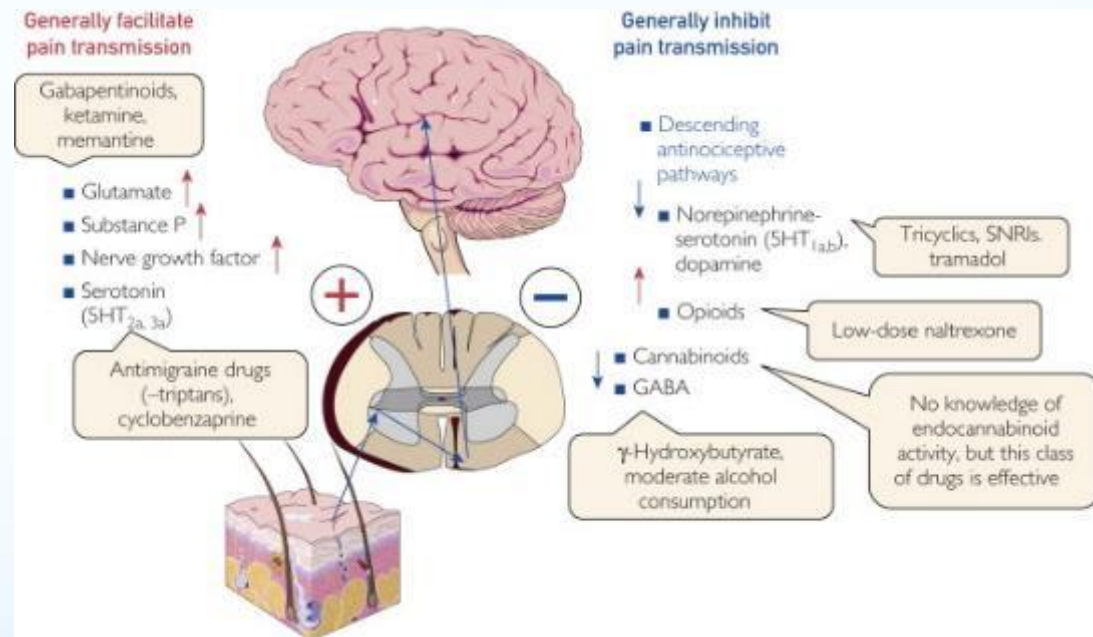
- Dysfunction of CNS pain processing
  - Decreased endogenous analgesic systems
  - Inability to inhibit irrelevant sensory stimuli
  - Do not reduce pain felt after second painful stimulus



*SYMPOSIUM ON PAIN MEDICINE 2015, 90(5), P680-692.*

# Pathophysiology of FMS

- Potential cause: neurotransmitter alterations
  - Increased excitatory state
    - High substance P, glutamate, nerve growth factor
  - Decreased inhibitory state
    - Low GABA and dopamine
    - Dysregulation of serotonin and norepinephrine



*SYMPOSIUM ON PAIN MEDICINE 2015, 90(5), P680-692.*

# Pathophysiology of FMS

- Brain function alterations
  - Pain-sensitive brain areas over-activated on fMRI
    - Amygdala, insula, somatosensory cortex
      - Insula includes emotional processing of sensations (unpleasantness)
  - New connections between areas not normally involved in pain transmission
  - Reduction in total gray matter volume and increase in age-associated loss of gray matter → premature aging of brain
    - Worse with longer duration of disease
    - Look similar to depressed brains



# Pathophysiology of FMS

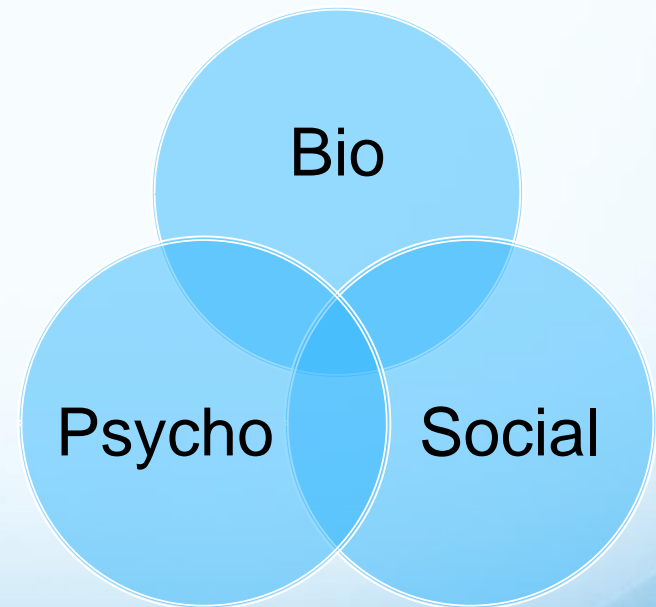
- Muscle dysfunction
  - Lactic acid buildup and mitochondrial dysfunction (lower ATP)
  - Overall capillary density lower – less blood flow
- Immune dysregulation
  - Pro-inflammatory cytokines (IL-6 and IL-8 elevated in sera)
  - Immune cell hyper-responsiveness: microglia in CNS
  - No autoimmunity, maybe...
- Sleep disorders
  - Alpha stage intrusion
  - Stage IV and REM reduced

# Comorbid Conditions

- IBS
- Interstitial Cystitis
- Dyspareunia/pelvic pain
- Migraines
- TMJD
- Joint hypermobility syndrome/EDS
- CFS/Myalgic Encephalomyelitis
- OSA, RLS, other sleep disorders
- Mood disorders: anxiety, depression, PTSD, OCD...
- Atopic disorders
- Raynaud's
- Autoimmunity – RA, SLE, AnkSpond, Sjögren's
- Thyroid dysfunction
- OA
- GERD
- HTN
- Cardiac disorders/arrhythmias
- Hyperlipidemia
- Obesity/physical inactivity

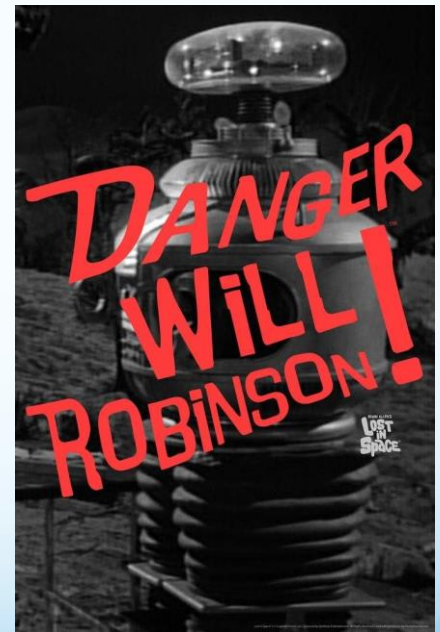
# FMS Triggers

- Can happen gradually or right after a trauma
  - Emotional
    - Adverse Childhood Experiences (ACEs)
    - Abuse
    - Job dissatisfaction/burn out
    - Poor support system
    - Relationship problems
  - Physical
    - Injury
    - Deconditioning
  - Infectious or other severe illness



# Why did this condition evolve?

- My hypothesis: sense danger quicker than before to avoid it
- Hypersensors of environment
  - Hypervigilance
  - Sight – photophobia
  - Hearing – phonophobia
  - Smell – heightened
  - Taste – super tasters?
  - Touch – hyperalgesia and allodynia
    - Hyperreflexia?



# This is NOT a diagnosis of exclusion

- Need a high index of suspicion
- Early diagnosis and treatment is important to prevent disability
- Keep active and involved in society → improve quality of life

# Differential Diagnosis

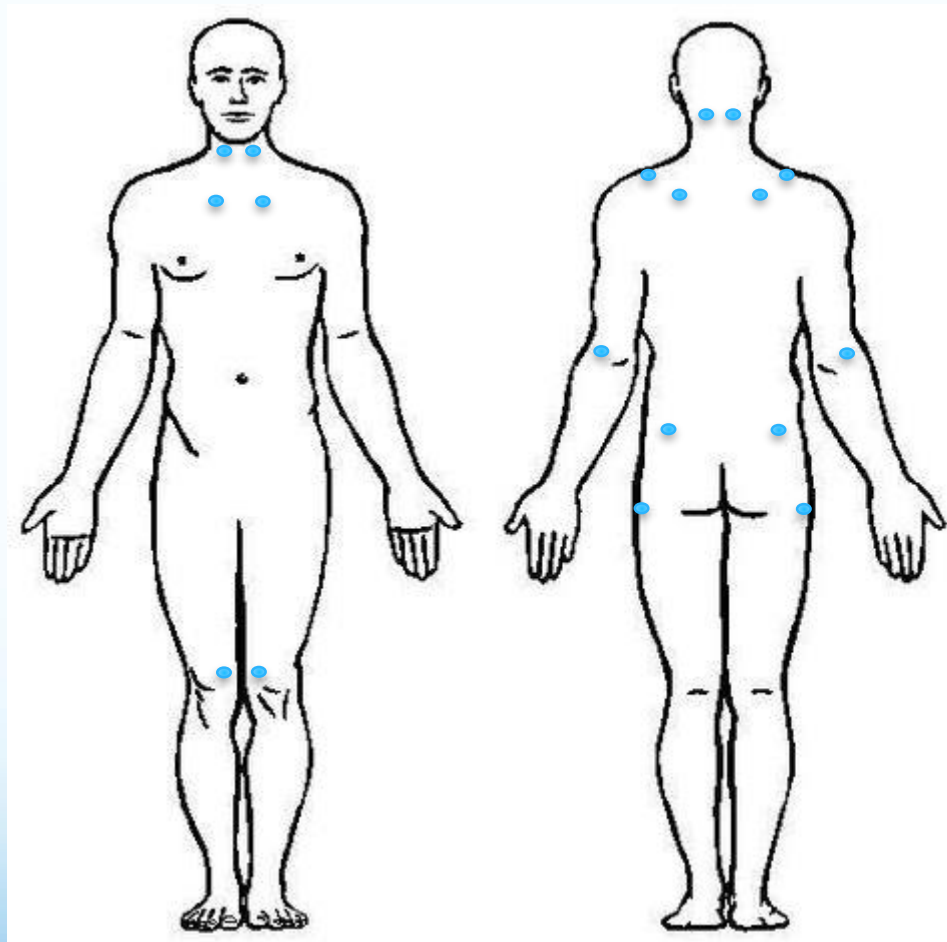
- RA – joint swelling, elevated ESR/CRP
- SLE – malar rash, renal/cardiac/pulmonary/neuro features
- PMR – older age at onset, elevated ESR/CRP, rapid response to glucocorticoids
- Polymyositis – muscle weakness, elevated muscle enzymes, abnormal EMG
- Spondyloarthritis – restricted spinal motion, elevated ESR/CRP
- Lyme – bullseye rash, joint swelling, serologic tests
- Hypothyroidism – abnormal TSH, pain not prominent
- Neuropathies – sensory/motor deficits, abnormal EMG

# Diagnostic Criteria for FMS: Old ACR Model

Widespread  
pain > 3 months

FMS if  
>11/18 tender  
points are  
positive

Presence of  
other clinical  
disorder does not  
exclude dx of  
FMS



CONS:

Males have higher  
pressure pain  
threshold than  
females

Skewed towards  
female prevalence

Tender points often  
incorrectly assessed  
or not assessed at  
all in primary care

No mention on non-  
pain symptoms

# Diagnostic Criteria for FMS: New ACR Model

- New ACR criteria (revised in 2010/11 and 2016)
  - Prevalence more equal between men and women, similar to other pain conditions
  - Generalized pain (at least 4/5 body regions)
  - Symptoms present at similar level  $\geq 3$  months
  - Diagnosis of FMS is valid irrespective of other diagnoses (can have FMS AND another disorder)
  - Widespread Pain Index (WPI): number of areas patient has pain over the last week (score 0-19)
  - Symptom Severity Scale (SSS): sum of severity of fatigue, waking unrefreshed and cognitive symptoms plus severity of general somatic symptoms (score 0-12)
  - WPI  $\geq 7$  and SSS  $\geq 5$ 
    - or WPI 4-6 and SSS  $\geq 9$
  - Fibromyalgia Severity (FS) scale is the sum of WPI and SSS



**Widespread Pain Index (WPI):** Note the number of areas in which patient has had pain over the last week. In how many areas has the patient had pain? Score range is 0-19.

*L Upper Region (1)*

- L jaw
- L shoulder girdle
- L upper arm
- L lower arm

*R Upper Region (2)*

- R jaw
- R shoulder girdle
- R upper arm
- R lower arm

*Axial Region (3)*

- Neck
- Upper back
- Lower back
- Chest
- Abdomen

*L Lower Region (4)*

- L hip (buttock, trochanter)
- L upper leg
- L lower leg

*R Lower Region (5)*

- R hip (buttock, trochanter)
- R upper leg
- R lower leg

## Symptom Severity Scale (SSS) score (range is 0-12)

Fatigue  
Waking unrefreshed  
Cognitive symptoms

For each of the 3 symptoms above, indicate the level of severity over the last week using the following scale:

0 = No problem

1 = Slight or mild problems, generally mild or intermittent

2 = Moderate, considerable problems, often present and/or at moderate level

3 = Severe: pervasive, continuous, life-disturbing problems

The SSS score is the sum of the severity score of the 3 symptoms (0-9) plus the sum of the number of the following symptoms the patient has been bothered by that occurred during the previous 6 months (0-3):

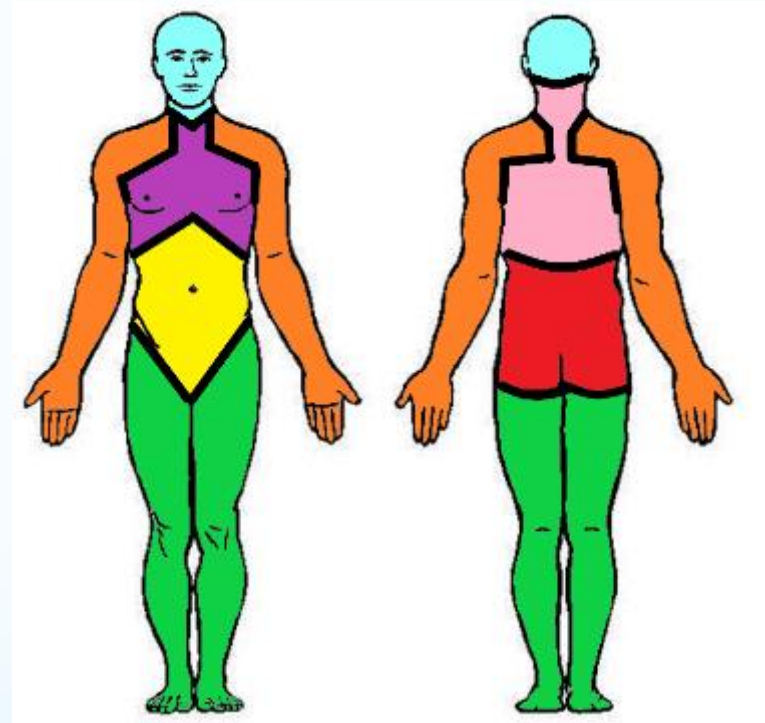
1) Headaches (0-1)

2) Pain or cramps in lower abdomen (0-1)

3) Depression (0-1)

# Newest Diagnostic Criteria for FMS

- AAPT (ACTION-APS Pain Taxonomy) working group
- History of at least 3 months of BOTH multisite pain at 6/9 possible sites AND moderate to severe problems with sleep or fatigue
- Do not require enumeration of tender points at defined sites by physical exam
- Other disorders that cause pain or related symptoms does not exclude the possibility of FMS
  - Must fully evaluate any other condition that could be causing those related symptoms or pain



Sites: Head, L arm, R arm,  
Chest, Abdomen, Upper back  
and spine, Lower back and spine,  
L leg, R leg

# HPI: Listen to your patient!

- FATIGUE
  - Flu-like symptoms
  - “I hurt all over”
- Cognitive dysfunction: “Fibro Fog”
  - Working memory impairment
  - Poor concentration
  - Word-finding difficulties
  - Disorganized/slow thinking
- Poor quality of sleep and/or insomnia
- Migrating pains and paresthesias
  - Muscle twitching
  - Arthralgias: TMJD, morning joint stiffness



# HPI: Listen to your patient!

- Neuro complaints: headaches, migraines, dizziness, blurry vision
- GI complaints: nausea/vomiting, GERD, abdominal pain/cramping, diarrhea, constipation
- GU complaints: urinary frequency, urinary urgency
- Anxiety and depression
  - Chest pain
  - Catastrophizing
  - Perfectionism/neuroticism
  - Compulsive behavior
- Atopy and Environmental sensitivity
  - Bright lights, loud noises, cold, perfumes, chemicals

# Diagnosis

- Physical exam
  - Soft tissue is tender to palpation
    - Muscles, ligaments, tendons especially
  - Evaluate for other possible disorders that have similar symptoms
    - Joint assessment for synovitis (should be no joint damage!)
      - No overlying erythema, warmth, or swelling
    - Neurologic exam normal: no focal deficits
      - Might see findings suggestive of peripheral neuropathy or small-fiber neuropathy
      - Might see evidence of autonomic nervous system dysfunction: tachycardia, orthostasis, palpitations

# Diagnosis

- No specific lab abnormalities are diagnostic for FMS
- Do labs only to rule out other things
  - CBC
  - CRP or ESR to rule out inflammatory process
  - RF, ANA, etc. not necessary for FMS patients
  - Vitamin deficiencies: B12, folate for paresthesias, D3 for depression/fatigue
  - TSH for thyroid disease
  - CK for inflammatory muscle disease
  - Iron studies?
  - CMP?

# Diagnosis

- No characteristic radiographic findings in FMS
  - Imaging not necessary unless you are sure it's something else!
- Might consider sleep study to check for sleep disorders
- Might consider psych referral for undiagnosed mental health problems
- Other referrals: physiatry, physical therapy, pain specialists



# Treatment

- Need multimodal approach tailored for individual patient
  - Patient Education!!!
  - Non-pharmacologic – exercise program, CBT, sleep hygiene
  - Pharmacologic (2nd line, only if needed)
- Goals: maintain/improve function, improve quality of life, manage symptoms
  - Teal = shown to significantly improve FMS symptoms and recommended by EULAR (European League Against Rheumatism)

# FIRST: Patient Education

- Real illness!! Not “all in your head”
  - Validation, empathy, compassion
- Prognosis: benign, not progressive, not infectious
- Pathophysiology of central sensitization
  - Increased pain perception, fatigue, abnormal sleep, and mood disturbances
- Symptoms wax and wane, but pain/fatigue may persist
- Can have normal life with some modifications
  - Activity pacing, knowing your limits, listening to your body



Knowledge is  
Power

# Patient Education

- Treatment approaches
  - Patient's role in their treatment plan: taking ownership
  - Start with treating worst symptoms first
  - No “magic bullet” to cure it
  - No “one size fits all” approach either
  - Understand that meds help a little, not a lot
- Sleep hygiene and effects of poor sleep on function and pain
  - Treat any underlying sleep-associated disorders
    - OSA, PLMD, or RLS

# Patient Education

- Importance of treating comorbid mental disorders
  - Mood disorders especially
  - Managing physical and emotional stress to reduce flares
  - Fix maladaptive chronic illness behavior – CBT
- Good to educate family members as well
- No time to educate? Refer to internet-based programs!

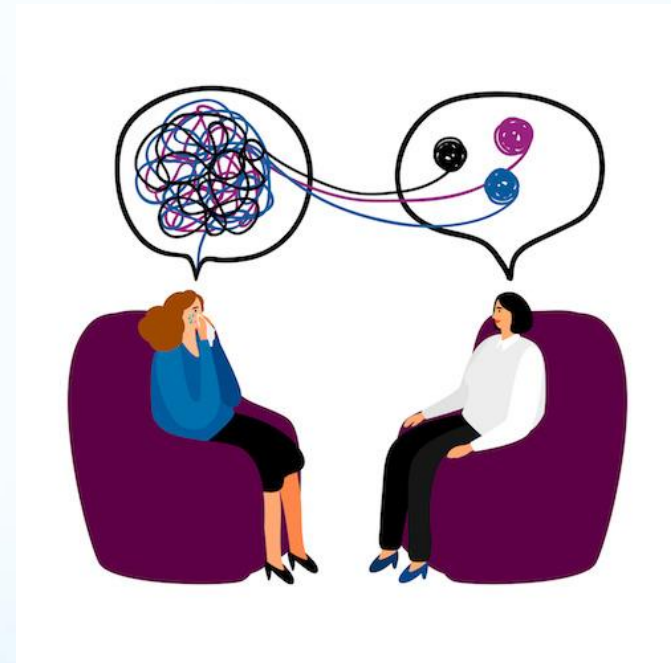


# SECOND: Exercise is key!

- **Low-impact Aerobic and Strengthening Exercise**
  - Start with low to moderate intensity (walking, swimming, cycling, water aerobics)
  - Graded exercise programs: increase intensity over time to goal of 30-60 minutes of moderate exercise at least 3 times weekly
- Strength training and stretching
  - Low weight and high reps
- Increases blood flow to release lactic acid buildup
- May have temporary increase in myalgias, but will get better!
- Improves: pain, overall function, sleep, mood, and quality of life

# THIRD: Psychotherapy

- Cognitive Behavioral Therapy (CBT)
  - Understand, recognize, and modify maladaptive thinking/behavioral patterns
  - Great for concurrent mood disorders
  - Face to face, online, books/CDs
  - Psych referral if possible
- Usually better and cheaper than medication!
- Improves: pain, overall function, sleep, mood, and QOL with lasting effects!



# FOURTH: Improve Sleep

- Restore sleep
  - Sleep hygiene
  - CBT for insomnia (CBT-I)
  - Treatment of comorbid sleep disorders
    - OSA, RLS, PLMD...
- Improves: pain, overall function, sleep, mood, and QOL



# Add-ons: Holistic Medicine

- Mindfulness-based stress reduction
  - Improve coping with pain
  - Improves: sleep, symptom severity, and perceived stress
- Meditative movement therapies
  - Yoga
  - Tai chi
  - Qigong
- Defined physical therapies
  - Acupuncture
  - Hydrotherapy





# Add-ons: Holistic Medicine

- **Weight Loss**
  - Gluten-free diet
    - Improves: GI symptoms
    - Not for everyone
  - Hypocaloric diet
    - Improves: symptom severity and pain (joints especially!)
    - Might be from IL-10 increase (anti-inflammatory)
  - Low FODMAP diet
    - Improves: GI symptoms (abdominal pain)

# Not Recommended by EULAR

- Biofeedback
- Hypnotherapy
- Guided imagery
- Transcranial Magnetic Stimulation (TMS)
- Topical capsaicin
- Massage
- Chiropractic
- Supplements (SAmE)
- Homeopathy

You can always try these and see if they help!

# FIFTH: Pharmacologic Therapy

- No strong evidence that they work well, only modest benefit
  - Very few continue meds due to lack of efficacy, side effects, or both
- May help with pain and sleep, not so much for fatigue or quality of life
- Choice depends on predominating symptoms, clinical experience, and patient preference
  - Only 3 FDA approved for FMS
- Start low and slow!!
  - Titrate to effectiveness and patient tolerability

# Tricyclics

- Amitriptyline
  - First line treatment (maybe)
  - Low cost
  - Start at 10mg at bedtime
  - Careful of side effects, especially in elderly
    - Anticholinergic side effects!
  - Improves: pain, fatigue, sleep, QOL
- Desipramine is alternative with fewer anticholinergic side effects

# SNRIs

- Next step in therapy
- Good for patients with severe fatigue and depression
- **Duloxetine** – FDA approved for FMS
  - Start at 20 or 30mg and double every 1-2 weeks
  - Goal is 60mg daily (no further improvement with higher doses)
  - Improves: pain and depressive symptoms, maybe fatigue
- **Milnacipran** – FDA approved for FMS
  - Start at 12.5mg daily and double weekly
  - Goal is 100mg daily
  - Improves: pain and fatigue

# SNRIs

- Venlafaxine
  - Lower cost, but short half-life causing withdrawal symptoms if missed dose
  - Unsure if effective
- Reboxetine
  - Inconsistent effectiveness
- Esreboxetine
  - Improves: pain, fatigue, and QOL

# Anti-convulsants

- **Pregabalin** – FDA approved for FMS
  - Start at 75mg bid and double every 1-2 weeks
  - Goal is 300-450mg daily
  - Can use with duloxetine – shown to be more effective than either alone
  - Improves: sleep and pain (maybe fatigue and QOL)
- **Gabapentin**
  - Low cost alternative to pregabalin
  - Start at 100-300mg at bedtime
  - For patients with poor sleep only
  - Careful of side effects
  - Improves: sleep and pain (maybe fatigue and QOL)

# Others

- Muscle Relaxants
  - Cyclobenzaprine
    - Similar to a TCA with minimal antidepressant effect
    - Good for mild/moderate symptoms
    - Improves: sleep mainly, small effect on pain
  - Tizanidine
    - Fewer DDIs than cyclobenzaprine
  - Baclofen
- Alcohol
  - Works to increase CNS GABA levels
  - Low-moderate consumption improved pain, function, and QOL
  - Heavy drinking did not help



# Others


- Naltrexone
  - Competitive opioid receptor antagonist and blocks innate immune receptor TLR-4
    - Might be anti-inflammatory in CNS
  - 4.5mg daily
  - Needs to be specially compounded
  - Improves: pain and depressive symptoms
- Anti-Parkinson's (NMDA Antagonists)
  - Memantine
    - 20mg/day (10mg bid)
    - Start at 5mg daily then increase by 5mg weekly
    - Improves: pain
  - Ketamine
    - Improves: pain
- Sleep aids
  - Melatonin
- Pramipexole
  - Comorbid RLS

# Not Recommended by EULAR

- SSRIs – usually not effective
  - Small improvements in pain, fatigue, QOL
  - Can try if cost is issue
- Cannabinoids
  - Inconsistent with effectiveness
  - Canadian guidelines for FMS management do include it for sleep problems
- MAO inhibitors
- Antipsychotics
- Corticosteroids
- Growth hormone
- Sodium oxybate


# What about opioids?

- NO!!!
- Opioids are ineffective for FMS pain
- Worse outcomes in FMS patients than those not taking opioids
  - Gradually taper them off (might take years)
- Some use **tramadol** as adjunct
  - Weak opioid with SNRI activity
  - Be wary of abuse
  - Improves: pain



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**ConsumerReportsHealth**  
American Society of Anesthesiologists<sup>™</sup>






**FOUNDATION**

**Medicines to relieve chronic pain**  
When you need opioids (narcotics)—and when you don't

# What about benzos or z-drugs?

- NO!!!
- Tolerance and dependence
- Zolpidem and other sleep meds not recommended long term
- Benzos are not first line for mood disorders!
  - Also not recommended long term

 <p><b>Choosing Wisely</b><sup>®</sup> <i>An initiative of the ABIM Foundation</i></p>	 <p>ABIM FOUNDATION</p>
 <p>AASM American Academy of SLEEP MEDICINE</p>	

**Sleeping pills for insomnia**  
They may not be the best treatment option

# What about OTC analgesics?

- Many patients self-medicate: NSAIDs especially
- Acetaminophen and NSAIDs are not effective for FMS pain
- Often prescribed as adjuncts, but no evidence they work
- If they do help your patient, make sure they are taking them safely



# Close Monitoring

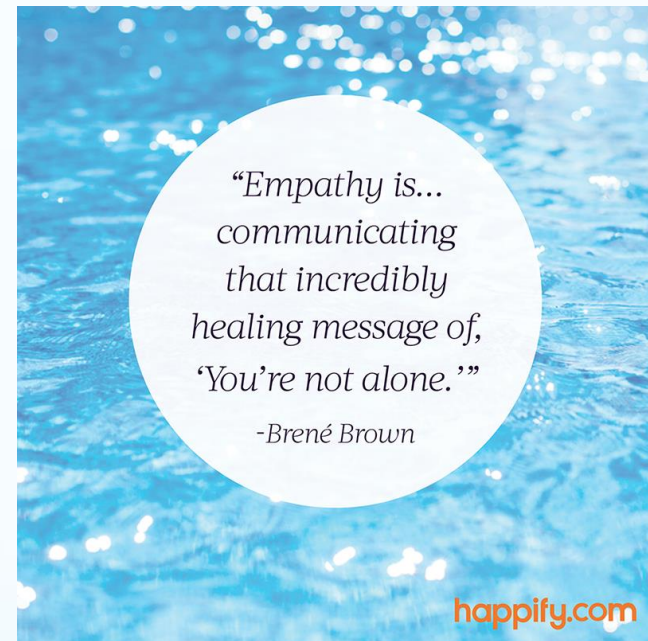
- Regular follow ups
  - Weekly or monthly
  - Symptom severity, functioning, response to treatment, adherence, and adverse effects
  - Greater outpatient engagement is protective against suicide in FMS patients
- Track daily or weekly symptoms to see progress
  - Can use the ACR Widespread Pain Index and Symptom Severity Score to track progress
  - Numbers have power!

# Set backs

- “Frequent fliers” can be emotionally overwhelming
  - Unrealistic expectations
  - Inability to cope
  - Noncompliance
- Flares happen so be prepared
  - Find triggers, reduce stress, relaxation exercises, pleasant activities, resting
- Feeling discouraged because you “can’t fix them”
  - Not all treatments work for every fibro patient
  - You just have to find your patient’s “cocktail”
  - Some have better outcomes than others

# You can do it!!

- Most are thankful for help and that you listened
- Treating FMS is a marathon, not a sprint
- You can change their lives for the better!! 😊





# Take Home Points

- Fibromyalgia is a chronic widespread pain disorder characterized by dysfunctional CNS pain processing
- Clinicians need to have a low index of suspicion for fibromyalgia and not treat it as a diagnosis of exclusion
- Utilize non-pharmacological treatment regimens that are tailored to each patient first, then pharmacological
- Close follow up, empathy, and support are key for an effective provider-patient relationship and treatment success

# Post-test Question #1

- Which of the following neurological symptom is characteristic of fibromyalgia?
  - Apraxia
  - Aphasia
  - Allodynia
  - Ataxia

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# Questions?

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