

***In The Name of God***

**Saman Asadi, M.D.**

**Anesthesiologist, Fellowship in Chronic Pain  
Shiraz University of Medical Sciences**

# FIBROMYALGIA

**SPATIAL DISORIENTATION**

**MEMORY PROBLEMS**

**IRRITABLE BOWEL**

**ATTENTION DEFICIT**

**RASHES AND ITCHING**

**CHANGES IN VISION**

**RESTLESS LEG SYNDROME**



**WIDESPREAD PAIN**

**MORNING STIFFNESS**

**SEVERE ALLERGIES**

**CHRONIC PAIN**

**BRAIN FOG**

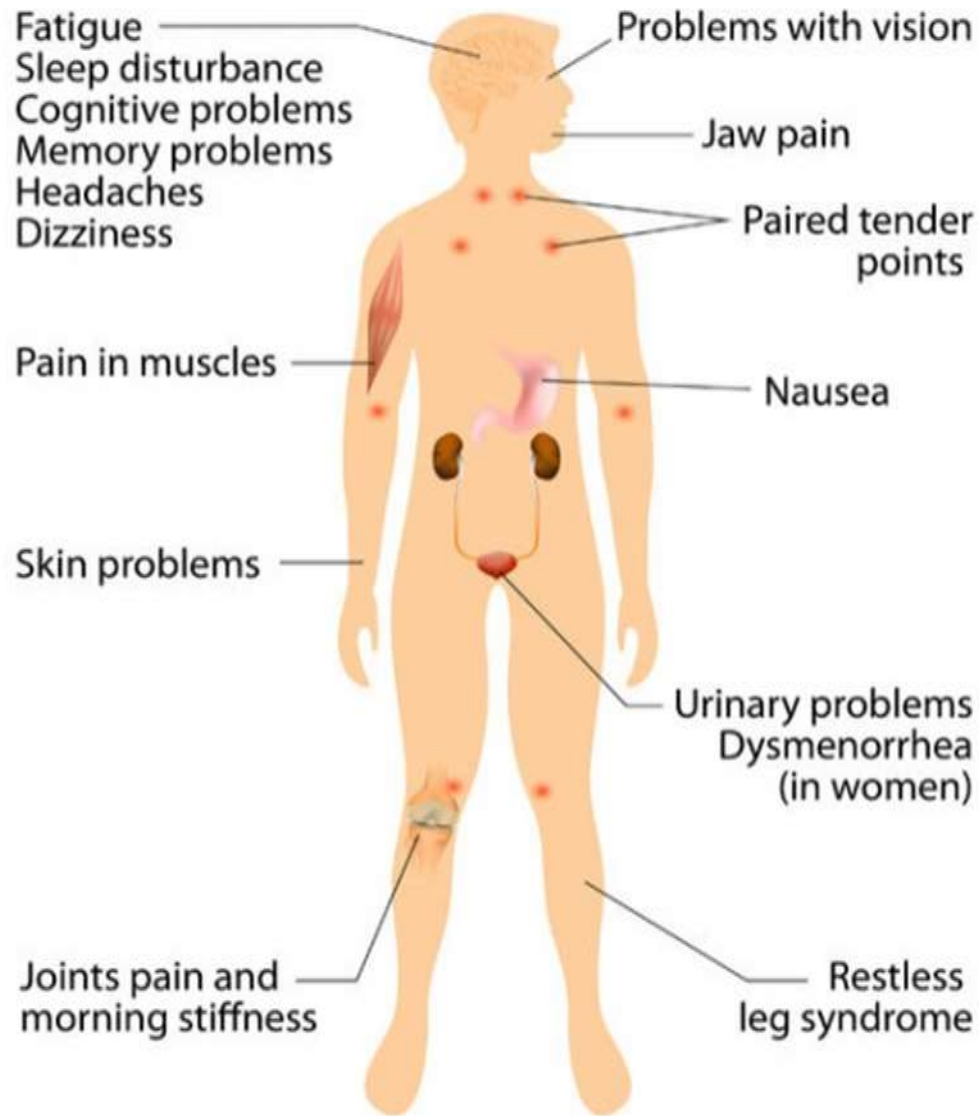
**CHRONIC FATIGUE**

**HEART PALPITATIONS**

***Fibromyalgia***, a condition affecting the **central nervous system**, causes **widespread pain** as well as other symptoms—such as **sleep disruptions**, fatigue, and **difficulty concentrating**—that adversely affect the patient's quality of life.

There is **no specific diagnostic test** for fibromyalgia,  
but  
a **variety of tools** are used to evaluate the patient's  
symptoms in order to confirm the diagnosis

# Fibromyalgia





**fatigue**



**brain fog**



**depression**



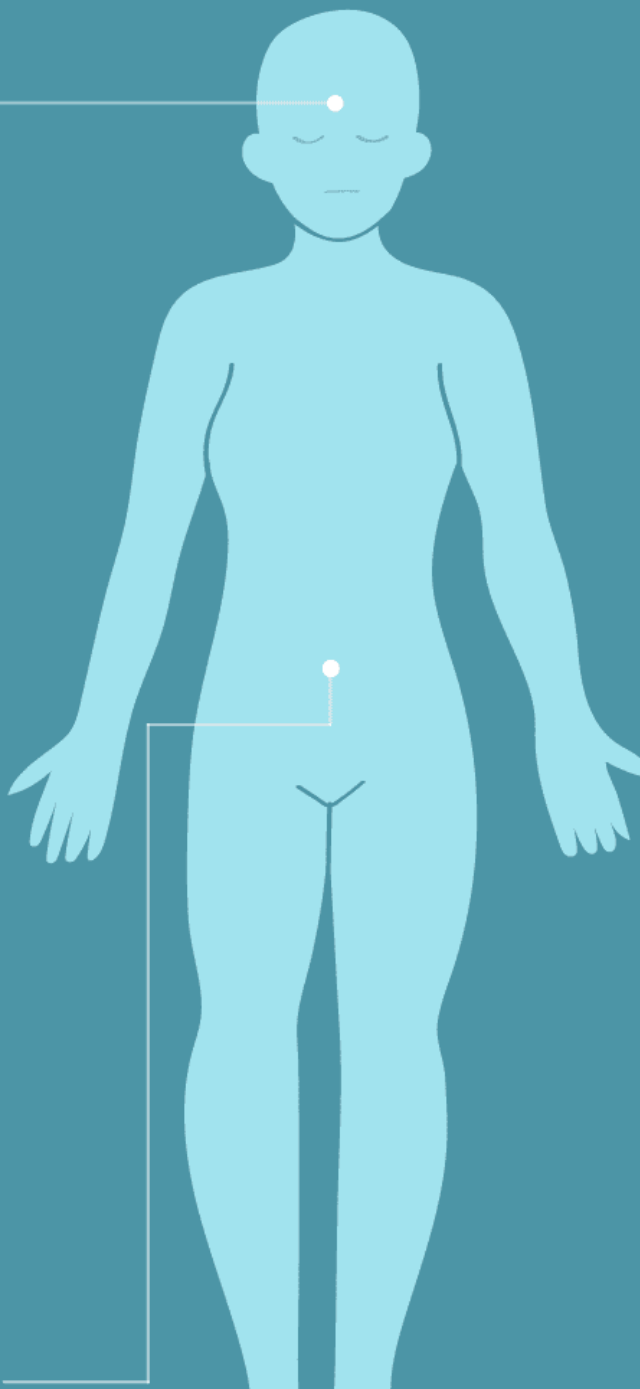
**chronic  
widespread  
pain**

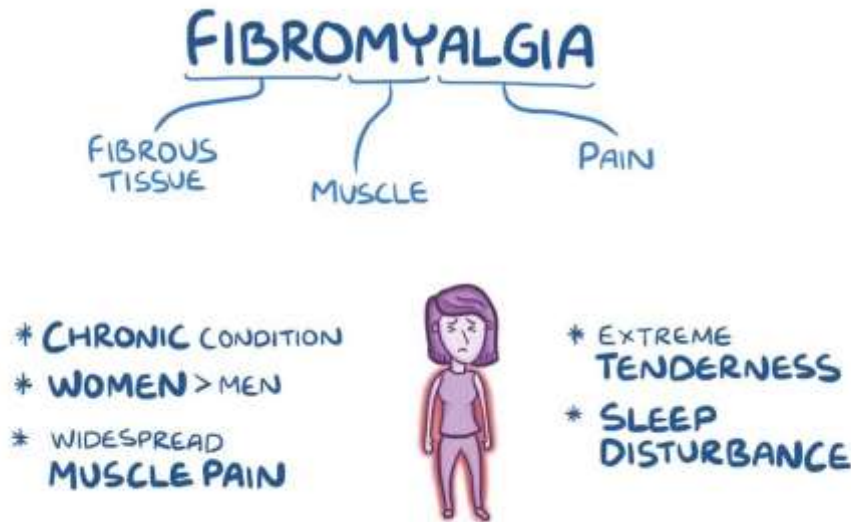


**muscle and  
joint issues**



**digestive issues**



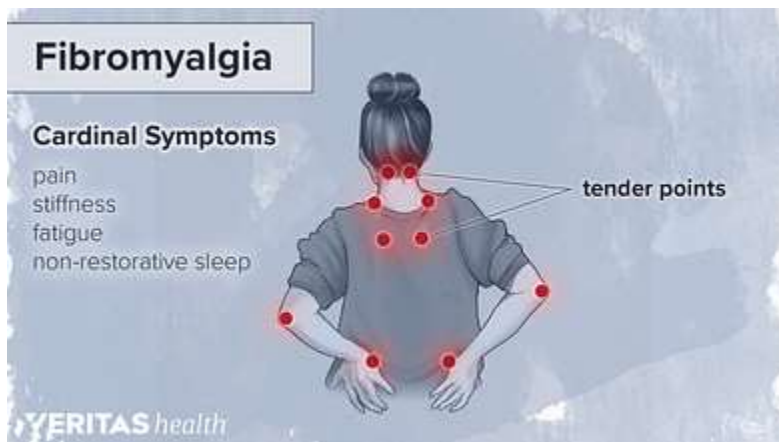


Although **several classes of medications**, such as **antidepressants**, are useful for treating fibromyalgia pain and other associated symptoms, nonpharmacologic treatments such as **exercise**, **mindfulness** techniques, **acupuncture**, and others have been shown to be equally effective—if not more effective—options.

**Fibromyalgia** is a chronic, disabling condition that encompasses musculoskeletal pain, **fatigue**, **depression**, and **sleep disturbances**.

It can significantly worsen the patient's **quality of life** and adversely affect **memory** and the ability to **learn** and **concentrate**

(a phenomenon known as dyscognition or “fibro fog”)



In some individuals,  
fibromyalgia is **triggered by** a **ph**ysical or **ps**ychological event or  
disorder;  
in others, it develops **gradually with no precipitating** cause.

Although fibromyalgia can occur **at any time of life**, even in  
childhood, **onset is usually in middle age**, and the likelihood  
**increases with age**.

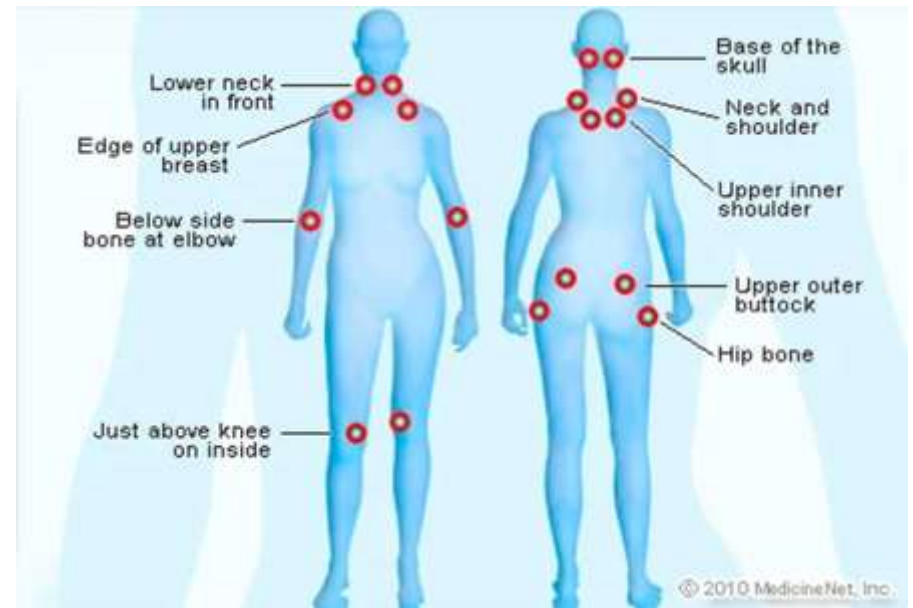
A **family history** of fibromyalgia may play a part in the  
development of the disorder.



# ETIOLOGY

The primary symptom of fibromyalgia is **chronic, widespread pain**.

Additional signs and symptoms may include stiffness; fatigue; **de**pression; **an**xiety; **ins**omnia; **hea**daches; **ting**ling or **num**bness in the hands or feet; **rest**less legs syndrome; **ir**ritable bowel syndrome; **tem**poromandibular joint disorder; and **sen**sitivity to light, temperature, and loud sounds.



**Fibromyalgia** is **two times more** likely in **women** than in men.

Other potential **risk factors** include age, rheumatoid arthritis, lupus, obesity, repetitive injuries, and traumatic or stressful or events.

Some studies have suggested a **genetic component**. One such study that compared fibromyalgia patients with healthy controls showed a **significant difference in cerebral pain processing due to polymorphisms in the mu-opioid receptor gene**

## EPIDEMIOLOGY :



The CDC has reported that **4 million U.S. adults—roughly 2%** of the population—have fibromyalgia

This condition was originally classified as an inflammatory musculoskeletal disease, but there are no inflammatory markers for fibromyalgia, and it has now been shown to primarily affect the central nervous system.

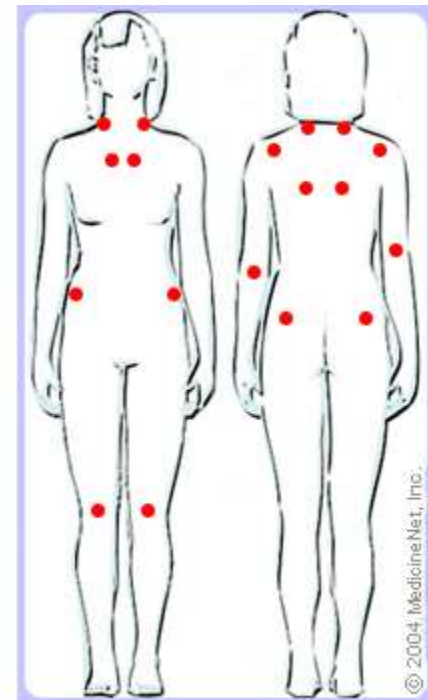
**5 Complications of fibromyalgia** may include hospitalizations and higher rates of other rheumatic conditions, major depression, and suicide

# DIAGNOSIS

Currently there are **no specific diagnostic tests** for fibromyalgia, but a review of the patient's medical history, physical examination, x-rays, and bloodwork can help **rule out other causes of widespread pain**.

Subjective tools, some of which are the Visual Analogue Scale, the Fibromyalgia Impact Questionnaire, and the Hospital Anxiety and Depression Scale, may be used to determine the severity of fibromyalgia symptoms.

One potential difficulty in fibromyalgia diagnosis is that a patient could have **condition that mimics fibromyalgia** (obstructive sleep apnea, Lyme disease, arthritis)



**Tender Points of  
Fibromyalgia**

**Table 1**

## Diagnostic Criteria for Fibromyalgia

**A patient is diagnosed with fibromyalgia when all of the following criteria are met:**

1. Generalized pain, defined as pain in at least 4 of 5 regions, is present.
2. Symptoms have occurred at a similar level for  $\geq 3$  months.
3. WPI score is  $\geq 7$  and SSS score is  $\geq 5$ , or WPI and SSS scores are  $\geq 9$ .

---

*SSS: Symptom Severity Scale; WPI: Widespread Pain Index.  
Source: Reference 7.*

## TREATMENT

There is **no cure for fibromyalgia** at present, but treatments are **available that can reduce symptoms**.

**Pain is typically the main symptom**, but other symptoms may include **depression**, **anxiety**, **sleep disorders**, and various other conditions.

Both **pharmacologic** and **nonpharmacologic** approaches to treatment are recommended depending on the patient's signs and symptoms.

Options include antidepressant use, sleep management, exercise, fibromyalgia support group participation, acupuncture, and stress-reduction activities.

It is important to note that **some prescribed medications**, while effective at **first**, may show reduced efficacy **over time**.

In such cases, it is recommended that the patient be **weaned off the medication and then slowly initiated on a replacement**. It may be necessary to attempt this **multiple times** until the right combination of medications is found

## Pharmacologic

Medications currently indicated for the treatment of fibromyalgia include **duloxetine**, **milnacipran**, and **pregabalin**.

Medications with off-label use include **amitriptyline**, **cyclobenzaprine**, **gabapentin**, **fluoxetine**, and **venlafaxine**



**Table 2****Pharmacologic Treatment Options for Fibromyalgia**

<b>Drug</b>	<b>Dosage</b>	<b>Common/Serious Side Effects</b>	<b>Major Precautions</b>
<b>Labeled Drugs</b>			
Duloxetine (SNRI)	30 mg po once daily for 1 wk; may increase to 60 mg/day	Abdominal pain, constipation, drowsiness, ED, suicidal ideation, SS	Platelet aggregation may be impaired due to platelet serotonin depletion. Additional serotonergic agents may increase SS risk
Milnacipran (SNRI)	12.5 mg po on day 1, 12.5 mg bid on days 2-3, 25 mg bid on days 4-7, then 50 mg bid; may increase to 100 mg bid	Constipation, headache, insomnia, ED, suicidal ideation, SS	Platelet aggregation may be impaired. Additional serotonergic agents may increase SS risk
Pregabalin (anticonvulsant, analgesic, anxiolytic properties)	75 mg po bid; may increase to 225 mg bid	Ataxia, constipation, drowsiness, weight gain, angioedema, confusion, anaphylaxis, GI bleed, suicidal ideation	Concomitant use with other CNS and/or respiratory depressants may exacerbate these symptoms
<b>Off-Label Drugs</b>			
Amitriptyline (TCA)	10 mg po daily hs; may titrate to 50 mg/day hs	Blurred vision, constipation, memory impairment, weight gain, ED, suicidal ideation, SS, torsades de pointes	Concomitant use with anticonvulsants may increase CNS depression and lower seizure threshold. Concomitant use with CNS and/or respiratory depressants may exacerbate these symptoms. Additional serotonergic agents may increase SS risk
Cyclobenzaprine (skeletal muscle relaxant)	Dosages from clinical trials range from 1 mg-4 mg po hs	Sedation, dry mouth	Concomitant use with CNS depressants may exacerbate these symptoms. Additional serotonergic agents may increase SS risk
Fluoxetine (SSRI)	20 mg po once daily; may increase to max 80 mg/day as tolerated	Transient nausea, anorexia, drowsiness, insomnia, ED, suicidal ideation, SS, QT prolongation	Platelet aggregation may be impaired due to platelet serotonin depletion. Additional serotonergic agents may increase SS risk. Fluoxetine is a strong inhibitor of CYP2D6, CYP3A4

*(Continued)*

## Pharmacologic Treatment Options for Fibromyalgia (cont'd)

Drug	Dosage	Common/Serious Side Effects	Major Precautions
<b>Off-Label Drugs (cont'd)</b>			
Gabapentin (anticonvulsant, analgesic)	300 mg po hs; may titrate to 2,400 mg/day	Headache, dizziness, sedation, nausea	Concomitant use with CNS and/or respiratory depressants may exacerbate these symptoms
Venlafaxine (SNRI)	Extended-release: 37.5 mg or 75 mg po once daily; may titrate to clinical response	Headache, insomnia, drowsiness, ED, suicidal ideation, SS	Platelet aggregation may be impaired due to platelet serotonin depletion. Additional serotonergic agents may increase SS risk

CNS: central nervous system; ED: erectile dysfunction; GI: gastrointestinal; max: maximum; SNRI: serotonin-norepinephrine reuptake inhibitor; SS: serotonin syndrome; SSRI: selective serotonin reuptake inhibitor; TCA: tricyclic antidepressant.

Source: Reference 9.

## Anti-Inflammatory Medications:

Patients sometimes self-medicate with **nonsteroidal anti-inflammatory** agents such as ibuprofen or naproxen or are prescribed corticosteroids to treat peripheral pain. However, evidence indicates that these medications are **ineffective for treating fibromyalgia pain**

## Antidepressants:

Antidepressants were found to decrease pain, reduce sleep disturbances, enhance mood, and increase HRQOL.

Except for amitriptyline, there was little evidence of improvement in fatigue.

**Amitriptyline** improved pain, fatigue, and sleep disturbances but did not improve depressed mood (it was speculated that the doses used were too low to have an effect).

**Fluoxetine** and **paroxetine** produced a decrease in pain and a small effect on depressed mood and HRQOL, but they had no effect on fatigue or sleep.

**Duloxetine** and **milnacipran** lessened pain and sleep disturbances, and duloxetine resulted in improvements in depressed mood and HRQOL.

Based on these findings, **short-term use of amitriptyline or duloxetine was recommended.**

For patients whose **chief symptoms are depression and/or anxiety**, an antidepressant such as duloxetine or fluoxetine, based on current evidence, should be used.

If **sleep-related difficulties are a bigger** problem, amitriptyline may be a better option

## Cannabis:

Data on the use of cannabis for the treatment of fibromyalgia are limited. Nabilone is a synthetic cannabinoid approved only for treating refractory nausea and vomiting in patients undergoing chemotherapy.

Although nabilone has been shown to have some benefit for sleep improvement, anxiety reduction, and HRQOL (0.25 mg-2 mg/day), evidence is weaker compared with first-line treatments for fibromyalgia. Side effects include dizziness, poor coordination, dry mouth, and ataxia.

The Canadian Rheumatology Association states that it does not endorse the use of dried cannabis and currently recommends against it unless standard treatment has failed.

## Opioids:

Although opioids are used to treat many different types of pain, their use for fibromyalgia remains **controversial** at best.

**Not much data exist to support** the use of opioids, and other medications are available that can effectively alleviate the symptoms of fibromyalgia without potentially causing debilitating adverse effects such as mood disturbances, constipation, sedation, mental clouding, and dependence. In as little as 1 month, regular use of opioids can produce **opioid-induced hyperalgesia**.

**Tramadol**, which has a **different mechanism of action** than other opioids, has been **used to treat fibromyalgia pain**. In addition to binding to **mu-opioid** receptors, it also **inhibits both serotonin and norepinephrine reuptake**. Tramadol is also **less likely to produce dependence**.

**Hyperalgesia (enhanced sensitivity to pain) is not** a reported adverse effect of tramadol. Although tramadol is not indicated for the treatment of fibromyalgia, dosages of **50 mg to 400 mg daily** have been reported.

## Combination Therapy:

A meta-analysis of 16 studies that used various two-drug combinations for treatment of fibromyalgia pain reported that three combinations (**melatonin-amitriptyline**, **fluoxetine-amitriptyline**, and **pregabalin-duloxetine**) produced a **greater reduction in pain** compared with monotherapy alone.

It has been suggested that patients who exhibit polygenic chronic illnesses may be treated with combinations of medications based on their **different mechanisms of action**



## **Nonpharmacologic Treatments :**

- **relaxation therapy (RT)**
- **Exercise**
- **Acupuncture**

## Fibromyalgia :



Is a **chronic** condition that can cause **widespread pain**, depression, anxiety, and a host of other symptoms.

The **goals of therapy** should be to **lessen** the severity of symptoms and to **improve** HRQOL;

**Not focusing solely on pain** management is a recipe for failure.

Pharmacists should discuss with patients not only the prescribed **medications** but also the various nonpharmacologic options, and they should encourage patients to find the best avenue for their care. For many patients, **nonpharmacologic** options often provide the greatest symptom relief. **Exercise** has demonstrated **the biggest** improvement in fibromyalgia symptoms including **pain**, **depression**, **anxiety**, and **sleep problems**.

**THANKS**