Fibromyalgia is a common chronic pain disorder characterized by widespread musculoskeletal pain, fatigue, sleep disturbance, and cognitive difficulties that affects an estimated 4-5% of the general population.\(^1\) In clinical practice, despite the syndrome’s common prevalence, the diagnosis remains challenging with delays in diagnosis and treatment.\(^2\) A large-scale international survey of 1,622 physicians reported that, while a majority had seen a patient with fibromyalgia in the last two years, 53% had difficulty diagnosing fibromyalgia, 54% reported their fibromyalgia training was inadequate, and 32% considered themselves not knowledgeable about the condition.\(^3\) This inadequacy is further evidenced in primary care where up to one in 20 patients report FM symptoms but 46% of primary care physicians report uncertainty with diagnosing fibromyalgia.\(^4,5\) Recent publications recommend increased efforts for fibromyalgia education in health care providers.\(^6-9\) The present review discusses the evolution of fibromyalgia diagnosis and provides a guide for the clinical implementation of the latest diagnostic criteria from the American College of Rheumatology (ACR).

### Early Descriptions of Fibromyalgia

Early reports of fibromyalgia-like illnesses date back to the 16\(^{th}\) century. French physician Guillaume de Baillou introduced the first modern descriptions of “rheumatism” and fibromyalgia in his *Liber de rheumatismo et Pleuritide dorsali*.\(^10\) Over time, symptoms of widespread myofascial pain became known as “muscular rheumatism” as physicians started to differentiate between articular and non-articular musculoskeletal disorders.\(^11\)

In the 19\(^{th}\) century, several authors began to identify chronic pain syndromes of muscular origin.\(^12\) One of the earliest to localize widespread pain to the muscles was William Balfour, a surgeon from Edinburgh, who championed the idea that inflammation of muscle and connective tissue was the source of chronic musculoskeletal pain.\(^13\) However, it was Balfour’s later findings in 1824 that mark a significant milestone in the development of the fibromyalgia concept and future diagnostic criteria: regions of focal tenderness called tender points.\(^14\)

Following observations that pain could radiate from tender points, the referred pain concept began to draw the attention of those studying muscular rheumatism. In 1841 French pediatrician Francois Louis Isidore Valleix proposed that muscular rheumatism was a form of neuralgia after observing referred pain from tender points ran in close proximity to nerve routes.\(^15\) Others suggested that the pain radiation was independent of nerve trajectory and implicated muscle hypertonicity or nerve hyperreactivity.\(^16-17\) In 1858, Thomas Inman speculated that tender points were caused by localized functional changes such as muscle spasms. Alternatively, Cornelius was one of the earliest to describe a relationship between musculoskeletal pain and psychological factors with the proposition that “nerve points” were hyper-reactive nerve endings reactive to physical and emotional stimuli.

Psychological contributions to myofascial pain, however, would not be explored until after the 19\(^{th}\) century due to a majority emphasis on underlying muscle or connective tissue processes. The muscle callous theory claimed that exudative processes led to muscle fiber atrophy and replacement with connective tissue.\(^18\) In 1904, British neurologist Sir William Gowers first used the term “fibrositis” to describe fibrous tissue inflammation and studies performed by Stockman identified inflammatory changes in muscular nodules supportive of muscle pathophysiology.\(^21,22\) While not reproducible in later studies, Stockman’s findings solidified fibrositis as the favored diagnostic term for chronic myofascial pain and the misnomer persisted throughout fibrositis research in the 20\(^{th}\) century.

In the late 1930’s and early 1940’s interest in psychological factors increased, particularly in response to the mental health consequences of war. Reports documenting the frequent occurrence of fibrositis in 24% to 52% of World War II soldiers resulted in coinage of the term “psychogenic rheumatism” and the theory that fibrositis may be a psychological disorder.\(^23,24\)

As the medical community became increasingly interested in fibrositis, doubt surrounding the syndrome’s existence began to dissipate. However, the syndrome remained a neglected miscellany of symptoms despite growing clinical acceptance. In the 1968 article *Fibrositis*, Traut linked together many of fibromyalgia’s common features including chronic fatigue, widespread pain, chronic headaches, disturbed sleep, and tender points.\(^25\) At the time, Traut’s publication was monumental in unifying many of the syndrome’s seemingly unrelated, yet hallmark symptoms and paved the way for fibromyalgia becoming recognized as its own entity.
In 1977 Smythe and Moldofsky proposed the first diagnostic criteria in their seminal ‘Two contributions to the understanding of the ‘fibrositis’ syndrome’ which required “widespread pain lasting longer than three months, disturbed sleep with morning fatigue and stiffness, and a decreased pain threshold” quantified by the presence of at least 12 of 18 possible tender points. The 1977 criteria were the first to objectively diagnosing fibromyalgia with a focus on quantifiable measures and sparked a number of subsequent publications. However, some argued that Smythe and Moldofsky’s level of tenderness needed to achieve a diagnosis was unrealistic in clinical practice and this concern was reflected in other investigators’ reduction of the number of tender points required for diagnosis.

The term “fibromyalgia” was introduced by Yunus et al. who also proposed the first formal set of diagnostic criteria. The requirements included pain and stiffness in three body regions lasting for at least three months, the presence of four or five tender points, and, dependent on the number of tender points, varying levels of: poor sleep, fatigue, headaches, irritable bowel, anxiety, swelling, tenderness, and symptom exacerbation by weather or physical activity.

Discrepancies in subsequent diagnostic criteria led to debate over the relative contribution of tender points and psychosomatic symptoms. In response, the American College of Rheumatology (ACR) performed a multicenter study to standardize fibromyalgia classification criteria. The 1990 ACR classification criteria deemed 11 of 18 tender points sufficient to differentiate fibromyalgia patients from controls and introduced the requirement of chronic widespread pain (defined as 4-quadrant plus axial pain lasting for a minimum of 3 months) to differentiate fibromyalgia from localized musculoskeletal pain syndromes. It was concluded that primary and secondary-concomitant fibromyalgia were indistinguishable and made a fibromyalgia diagnosis “a valid construct irrespective of other diagnoses.” While the 1990 criteria factored in pain severity, it led to misclassification of regional pain syndromes as fibromyalgia. A controversial statement from the 2010/2011 criteria was inclusion of the statement that fibromyalgia diagnosis could not be made if the patient has a “disorder that could otherwise explain the pain.” This mistakenly implied that fibromyalgia could not be a comorbidity. The modified 2016 criteria reversed the language used in 1990 and added additional clarifications: “a diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.”

Despite significant advancements, the diagnostic criteria are not without limitations and require further validation. The addition of the WPI and SSS requires a more thorough history and assessment by health care providers. The inherent subjective nature of symptom assessment by both providers and patients also must be taken into account. There are arguments for and against self-report assessments in fibromyalgia diagnosis. Further investigation is needed to determine applicability and appropriateness in both research and clinical practice.

Beyond the Diagnostic Criteria: Pattern Recognition in Clinical Practice

While institution of diagnostic criteria for fibromyalgia has greatly benefited research, the American College of Rheumatology has not recommended definitive use in clinical settings and recommends physician discretion for clinical practice use. In the absence of directly translatable criteria, physicians need to recognize the clinical manifestations of fibromyalgia as part of the wider spectrum of central hypersensitivity syndromes.

One primary challenge in diagnosing fibromyalgia is the syndrome’s polysymptomatic nature. Fibromyalgia patients see an average of 3.7 physicians and accumulate numerous disjointed diagnoses prior to receiving a proper diagnosis two years after initial onset of symptoms. This leads to disgruntled patients, frustrated health care providers, and unintentional stigmatization of the disorder which further complicates care.

Growing evidence suggests fibromyalgia is a disorder that results from central sensitization and dysfunctional pain regulation. The centralized pain theory best explains the syndrome’s wide array of symptoms including multifocal pain, fatigue, insomnia, cognitive difficulties, and mood disturbances. Abnormal levels of neurotransmitters such as epinephrine, GABA, serotonin, glutamate, and substance P, may explain the psychiatric and psychosomatic symptoms, as well as sleep disturbances. Emerging research reveals the role of neuroinflammation in fibromyalgia. This type of
inflammation is described as neurogenic as it results from the release of neuropeptides from C-fibres with subsequent effects on blood vessels, sensory structures, and regional immune cells. Clinical features may be linked to neurogenic inflammation including tissue swelling, livedo reticularis, dermatographia, and allodynia.43

Due to the absence of definitive laboratory or radiographic testing, the diagnosis of fibromyalgia is clinical in nature. The clinician should obtain a detailed history of factors contributing to chronic pain. A central pain prone phenotype is associated with female sex, genetics, early life trauma, family history of chronic pain and mood disorders, personal history of chronic centrally mediated symptoms, behavioral patterns such as catastrophizing, and a lower mechanical pain threshold. 44 Fibromyalgia should be suspected in patients with chronic pain, diffuse hyperalgesia, and/or allodynia with signs of central sensitization. These patients commonly present with a history of multiple functional disorders diagnosed by other specialists including but not limited to irritable bowel syndrome, migraine headaches, temporomandibular joint disorder, interstitial cystitis, and endometriosis.

Laboratory testing to exclude mimickers of fibromyalgia may include: complete blood count (CBC), comprehensive metabolic panel (CMP), thyroid stimulating hormone (TSH), creatinine phosphokinase (CPK), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).

As emphasized in current diagnostic criteria, the presence of a second disorder does not exclude fibromyalgia or vice versa and all medical problems need to be addressed. Of particular importance is comorbid rheumatologic disorders with fibromyalgia. Analyzing six-months referrals, Fitzcharles and Boulos found only 34% accuracy of fibromyalgia diagnosis in patients referred for rheumatology consultation. Inflammatory rheumatologic conditions accounted for almost one-half of misdiagnoses.45 While science has yet to prove causality, the rate of comorbid fibromyalgia is high in connective tissue diseases and inflammatory arthritis including: 22.1% with systemic lupus erythematosus, 18-24% with rheumatoid arthritis, 14-16% in axial spondyloarthritis, and 18% in psoriatic arthritis. These are striking findings, when compared to rates of 4-5% in the general population.1,46-47 The higher comorbidity rates should caution providers to consider rheumatology referral when evaluating patients with joint pain and swelling, unusual rashes, photosensitivity, and family history of autoimmunity. When signs and symptoms of a connective tissue disease or inflammatory arthritis are present, pertinent labs include: CBC, CMP, ESR, CRP, TSH, CPK, as well as antinuclear antibody, rheumatoid factor, and anticyclic citrullinated peptide.

Confirmation of fibromyalgia diagnosis by a specialist may also be beneficial in the face of diagnostic uncertainty or patient concern. Receiving a diagnosis of fibromyalgia commonly brings relief to patients as it both explains and validates their symptoms. Proper diagnosis of fibromyalgia has economic benefits as well as health care costs decrease in fibromyalgia patients following diagnosis by rheumatologists.48

Conclusion

The past century has witnessed a significant growth in awareness and interest in fibromyalgia. Despite research advancements, complexities of the clinical diagnosis of fibromyalgia often leads to delays that directly impact patients’ quality of life. Fibromyalgia’s clinical diagnosis is based on widespread chronic pain, fatigue, and other centrally mediated symptoms. A diagnosis of fibromyalgia can be made appropriately in the primary care setting with careful evaluation including detailed medical history, thorough physical exam, and routine laboratory testing. Due to the high rate of comorbidity with rheumatologic disorders, health care providers should consider rheumatology referral in the appropriate clinical setting.

REFERENCES


