# COMMENTARY

# COMMENTARY: DIFFERENTIAL DIAGNOSIS OF FIBROMYALGIA SYNDROME: PROPOSAL OF A MODEL AND ALGORITHM FOR PATIENTS PRESENTING WITH THE PRIMARY SYMPTOM OF CHRONIC WIDESPREAD PAIN

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Fibromyalgia syndrome (FMS) remains an elusive condition of unknown etiology, in which patients report chronic widespread pain (allodynia or hyperalgesia) and a variety of other complaints including fatigue, sleep disorders, cognitive deficit, irritable bowel and bladder syndrome, headache, Raynaud's syndrome, bruxism, atypical patterns of sensory dysethesia, and other symptoms. Despite the name of the condition, *fibromyoalgia*, there are no data to support the hypothesis that FMS is a distinct pathologic disorder of the soft tissues. More recent data tend to support the notion that FMS is a disorder of the central nervous system pain processing pathways and not some type of primary auto-immune disorder of the peripheral tissues. It is quite possible that the term *FMS* is a poor choice of words, for it implies that patients with a variable symptom complex all have the same singular disease or disorder.

The diagnosis of FMS has been burdened by a controversial and problematic history since its inception in 1990, with a disturbing trend toward overdiagnosis in recent years. A recent study provided some evidence of the seriousness of improper FMS diagnosis, when a cohort of patients referred to a specialty rheumatology clinic with a tentative diagnosis of FMS were prospectively followed and the FMS diagnosis could only be confirmed in 34% of these patients.[1] The authors of this study were critical of the disturbing 66% diagnostic error rate and made these concluding remarks[1]: "There is a disturbing inaccuracy, mostly observed to be over-diagnosis, in the diagnosis of FMS by referring physicians. This finding may help explain the current high reported rates of FMS and caution physicians to consider other diagnostic possibilities when addressing diffuse musculoskeletal pain."

As the old adage goes "proper diagnosis is half the cure." With respect to the high reported rates of FMS in primary care and rheumatology clinics, this adage might be reversed to state "improper diagnosis is half the problem." The mere presence of widespread pain and fatigue should not be considered adequate grounds for making a de facto diagnosis of FMS, yet many times this is indeed the case.

At the heart of the overdiagnosis issue is the fact that a diagnosis of FMS is not based upon any laboratory or diagnostic tests, but rather upon 2 vague criteria. One of these criteria is chronic widespread pain and the other is the presence of a specific number of tender points.[2] Yet these 2 criteria are not specific to FMS; they may also be present in patients with many other medical conditions. Therein lies the problem; FMS is basically defined by 1 symptom—widespread pain, and 1 physical examination finding—areas of cutaneous tenderness (tender points). There are a number of medical diseases and syndromes that can manifest with these same symptoms, which could easily be misdiagnosed as FMS. It is interesting to note that this issue of overdiagnosis has apparently affected the principal author of the 1990 American College of Rheumatology (ACR) Criteria for Classification of Fibromyalgia Syndrome, who recently published an editorial article entitled "Stop Using the ACR Criteria in the Clinic."[3]

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The hallmark symptom that differentiates FMS from most other medical conditions is the pronounced tenderness to even the mildest palpation or physical touch. This extremely low tolerance to sensory stimulation fits the definition of allodynia, that is, the perception of pain to a nonpainful stimulus. Allodynia is quite pronounced in the classic presentation of FMS; it has been found to be multimodal (pressure, heat, electrical stimulation) and widespread throughout many body regions, not just the 18 predetermined sites chosen by the ACR consensus committee.[4] The presence of allodynia typically infers a disorder of nociceptive pathways within the central nervous system (central sensitization), and not an abnormality of peripheral tissues themselves. There are recent data to support the idea that the widespread allodynia associated with FMS is indeed caused by central nervous system dysfunction (central sensitization) as documented by functional magnetic resonance imaging (MRI) and positron emission tomography brain scans of patients with FMS[5] receiving innocuous sensory stimulation.

Several consensus conferences have addressed the issue of FMS diagnosis and treatment since the publication of the original 1990 ACR criteria and have all concluded that the patient with classic FMS presents with many other symptoms besides widespread allodynia.[6,7] It has been well established in the literature that patients with FMS are predominantly female (female/male ratio, 10-20:1), typically report nonrefreshing sleep, general fatigue, low energy, and experience concomitant anxiety and depression disorders. Fibromyalgia syndrome is reported to be part of a "wider syndrome" involving headaches, bruxism, irritable bladder, irritable bowel, sleep disorders, depression and/or anxiety disorders, cold sensitivity, Raynaud's phenomenon, exercise intolerance, cognitive deficit, and other symptoms suggestive of autonomic nervous system or neuroendocrine dysregulation.[6]

Most recently, a working clinical case definition of FMS for practitioners was published with updated diagnostic and treatment protocols as the result of a Canadian consensus conference.[7] Unfortunately, these "updated" criteria do not substantially add anything new to the literature; they still recommend the same 2 basic ACR criteria as being mandatory for making an FMS diagnosis, along with a laundry list of "additional clinical symptoms and signs" which include neurocognitive manifestations, fatigue, sleep dysfunction, autonomic and/or neuroendocrine manifestations, neurologic manifestations, and other symptoms. Some or all of these symptoms may be found along with the hallmark finding of widespread allodynia. This consensus conference concluded with some remarks about the need to start looking at a new conceptual model of FMS as a disorder with multiple subsets; a conceptual model that is long overdue in these authors' opinion.

A comprehensive review of the FMS literature was performed by the lead author (MJS) using the keyword "fibromyalgia" and searching the following online databases: Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, MEDLINE, CINAHL, MANTIS, and AMED. There is a serious lack of consensus on how to approach the diagnostic evaluation of patients with chronic widespread pain and especially on how to evaluate the medical condition of patients suspected of having FMS as the primary diagnosis. Of the few systematic reviews performed of the FMS literature,[8-10] only 3 basic treatment approaches appear to show a significant treatment effect in patients with FMS: (1) low-dose antidepressant medication; (2) mild exercise programs; and (3) cognitive behavioral therapy. The literature fails to delineate any specific cause(s) of this variable symptom complex known as FMS, which makes us question the validity of FMS as a separate and distinct clinical disorder.

## Discussion

A review of the FMS literature leads these authors to suggest that physicians need to take a hard look at the validity of the diagnosis of FMS as a single clinical entity and explore the alternate idea of multiple subsets of patients with myriad causes for their widespread pain and fatigue.

The literature leads the authors to hypothesize 4 basic subsets of patients who present with the primary symptom of chronic widespread pain. The first category represents the "classic" presentation of fibromyalgia syndrome, which these authors suggest is a psychosomatic illness that manifests with a number of associated somatic complaints. The remaining 3 categories represent other conditions that are often misdiagnosed as fibromyalgia, including medical diseases, functional metabolic disorders, and musculoskeletal disorders.

The term *classic* FMS is proposed to describe the type of patient who has widespread allodynia, headaches, sleep disorder, irritable bladder/bowel, multiple chemical sensitivities, bruxism, fatigue, and/or a variety of other symptoms. It is likely that this patient with classic FMS has a bona fide psychosomatic disorder, in which these physical signs and symptoms are the result of persistent hypervigilance and overactivation of limbic system pathways. When patients are misdiagnosed with FMS, it seems that the real cause of their widespread pain and fatigue is found within one or more of the following diagnostic categories: medical diseases, functional metabolic disorders, or musculoskeletal disorders.

Although this categorization scheme and algorithm are admittedly arbitrary and not formally validated, it provides a starting point for reexamining the conceptual model of FMS. Each of these different categories of the causes of widespread pain and fatigue will now be reviewed, followed by presentation of a diagnostic algorithm (Appendices A and B).

## Classic FMS

The term classic FMS represents the subset of patients whose physical symptoms are suggestive of an underlying mental illness, mediated by overactivity of the limbic system and hypothalamic-pituitary-adrenal axis, causing the multiple symptoms seen in the "classic" cases of FMS in rheumatology clinics. These classic cases probably represent the somatic manifestations of extreme emotional stress and/or psychologic illness, yet are distinct from a true somatization disorder in which there is no real physical illness. It is too simplistic to state that all cases of classic FMS merely represent a somatic manifestation of clinical depression or anxiety, because not all patients with depression or anxiety disorders experience the symptom of widespread allodynia with multiple tender points.

Yet it has been known for almost 20 years that patients with FMS often respond well (at least in the short-term) to low doses of antidepressant medications, suggesting that there is significant overlay between mood disorders and FMS. Recent studies are starting to implicate the role of the limbic structures (hippocampus, amygdyla, and hypothalamus) and neuroendocrine system in the production of FMS symptoms. One study showed differences in circadian cortisol release in FMS vs healthy controls, suggestive of overactivity of the hypothalamic-pituitary-adrenal axis in these patients.[11] Various types of thermal, mechanical, and electrical modalities have been applied to FMS and healthy controls, and consistently the FMS group shows signs of central sensitization.[12] Positron emission tomography scans and functional MRI studies of the brain activity of subjects with FMS vs healthy controls while they receive innocuous sensory stimulation have shown that the limbic structures of patients with FMS are activated by nonpainful stimuli which only activate the sensory cortex in healthy controls.[5]

Many studies have attempted to determine how much psychologic overlay exists in classic cases of FMS. One important study reviewed the prevalence of victimization and abuse in FMS, rheumatoid arthritis, multiple sclerosis, and chronic fatigue syndrome (CFS).[13] The results showed CFS and FMS patients had a significantly higher prevalence of emotional neglect and abuse, and of physical abuse, with a considerable subgroup experiencing lifelong victimization. Another study of 600 members of a health plan diagnosed with FMS showed an extremely high prevalence of past emotional, physical, and/or sexual trauma associated with the onset of FMS symptoms.[14] These findings support etiologic hypotheses suggesting a pivotal role for chronic stress in CFS and FMS and may have important therapeutic implications.

Patients with serious emotional or mental health issues often experience a significant sleep disorder, which probably represents a state of hyper-vigilance due to overactivity of the limbic system. This hyper-vigilance is commonly associated with posttraumatic stress and anxiety disorders, and may explain the well-documented alpha intrusion noted on electroencephalogram sleep studies of patients with FMS.[15] Lack of a normal sleep cycle is associated with hippocampal dysfunction, which manifests as short-term memory loss and cognitive deficit, both of which are common symptoms in patients with classic FMS. In lay terms, patients with FMS often use the term *fibro-fog* to describe this classic symptom of cognitive deficit.

It is not currently known exactly why certain patients with emotional illness or mood disorders will develop the characteristic symptoms of what is termed FMS, and why others with the same level of psychopathology do not experience these symptoms. There could be a combination of factors, including genetic predispositions that may in future research be shown to be associated with the production of FMS symptoms. A recent study of family members and probands of patients with FMS showed that reduced pressure pain thresholds aggregate in families, and FMS coaggregates with major mood disorders in families.[16]

The relevance for the clinician seeing these patients is the recognition that mental health and mood disorders may be the root cause of the symptoms of widespread pain, allodynia, sleep disorders, and cognitive deficit that could easily be misdiagnosed as FMS. It would seem appropriate for the clinician to refer these patients for cognitive behavioral therapy or other forms of psychologic counseling, rather than for physical therapy. A recent systematic review of the literature has shown that cognitive behavioral therapy is an effective treatment strategy for patients with FMS, along with mild exercise and low-dose antidepressant medication.[8]

## Medical Conditions Misdiagnosed as FMS

In patients presenting with generalized pain and fatigue, it is imperative that the clinician rule out the presence of any medical condition or disease that is known to cause these symptoms. Hypothyroidism, anemia, rheumatoid arthritis, Lyme disease, rheumatic auto-immune disorders such as ankylosing spondylitis or scleroderma, multiple sclerosis, and occult malignancy are some possible etiologies for symptoms of vague and diffuse musculoskeletal pain associated with pronounced fatigue. Most of this assessment comes in the form of serologic testing through a standard clinical laboratory, to include any or all of the following screening tests: complete red blood count (RBC) with white cell differential, thyroid function tests (T3, T4, TSH), SMA 24 or similar metabolic screening panel, C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR), Lyme test, and rheumatic profile (as indicated).

As simple as these screening tests may be to perform, it is not uncommon for clinicians to fail to have any laboratory

tests performed on their patient and still render a diagnosis of FMS. According to ACR guidelines and criteria, a diagnosis of FMS should not be rendered until all lab tests come back negative and fail to detect an organic reason for the symptoms.

A simple, rational approach to laboratory assessment of these patients includes an initial complete blood count as a screen for the common anemias, and the white cell differential to rule out infection or marrow disease. Obvious reasons for excessive fatigue, such as anemia, can be ruled out on the complete blood count by screening for low RBC count, altered hemoglobin, and abnormal RBC indices such as mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. An ESR or CRP test can help to confirm the presence or absence of systemic inflammation or infection. Although the ESR and CRP tests are nonspecific, extremely high values found on these tests may indicate the need for further serologic testing for underlying auto-immune rheumatic diseases or possible occult malignancy.

Thyroid function tests should be routinely performed in patients who present with the chief complaints of widespread pain and fatigue, to rule out overt hypothyroidism as the cause of these symptoms. Although the classic signs and symptoms of low thyroid function, including fatigue, weakness, cold intolerance, low temperatures, weight changes (usually weight gain), and depression are routinely considered clinically, common musculoskeletal signs and symptoms of hypothyroid include muscle pain, stiffness, muscle cramping, muscle weakness, paresthesia, arthropathy, and sluggish deep tendon reflexes are often not considered.[17] The incidence of musculoskeletal symptoms with hypothyroidism has been reported by Khaleeli et al[18] to be as high as 30% to 80% depending on the special interests of the diagnosing physician. This is extremely important as it is precisely these vague musculoskeletal symptoms that may drive the patient to the clinician initially. Many of these patients will likely be unaware that they have a thyroid condition, and if missed by the physician, their symptoms may inadvertently be misdiagnosed as FMS.

A standard serologic metabolic chemistry panel such as SMA 24 is useful to evaluate the overall systemic health of the patient presenting with widespread pain and fatigue. This panel includes serum fasting glucose, liver enzymes, cholesterol, blood lipids, and kidney function markers. Of course, these laboratory tests should be correlated with physical examination findings and other diagnostic tests. According to Hench,[19] 10% to 15% of unselected patients with FMS have isolated abnormal serologic test results without evidence of underlying connective tissue disease, which can often be misleading. If the physical examination findings are suggestive of joint pain and frank soft tissue inflammation, not simply increased pain perception in the soft tissues, additional serologic studies such as a rheumatoid panel and Lyme disease screening tests are warranted.

Again, it is important to note that if laboratory studies are positive for any of the above-noted medical conditions or diseases, a diagnosis of FMS is inappropriate. Stated bluntly, patients who have diseases that go undetected because of shoddy examination and investigation are likely candidates for a misdiagnosis of FMS to explain their constellation of symptoms. As a general rule, no patient should ever be given a diagnosis of FMS without a complete physical examination and basic screening laboratory testing to rule out the underlying medical conditions.

## Functional Metabolic Disorders Misdiagnosed as FMS

More subtle functional disorders may represent various types of subclinical disease states and disorders involving dysfunction of internal organs and metabolism, rather than true pathology. These functional disorders are often not on the busy clinician's radar screen and range the gamut from simple vitamin and mineral deficiencies, to more hidden functional disorders such as intestinal dysbiosis, subtle endocrine imbalances, reactive dysglycemia, post-viral immune suppression, and other conditions that are not readily apparent on standard laboratory screening tests.

Several nutritional deficiencies have been identified in patients with fatigue and widespread tenderness, in whom supplementation with various nutrients including B-vitamins, magnesium, and malic acid has shown positive results.[20-22] In mild to moderate cases of fatigue and widespread achiness, supplementation with the above nutrients may have a significantly positive clinical effect. However, patients with severe fatigue usually do not respond adequately to these supplements alone and require a more comprehensive functional approach. All of these functional disorders have the common denominator of potentially causing symptoms of low energy, fatigue, and widespread achiness, which are difficult to diagnose.

As was stated previously, thyroid function tests should be routinely performed in patients who present with the chief complaints of widespread pain and fatigue, to rule out overt hypothyroidism as the cause of these symptoms. However, more subtle presentations of thyroid dysfunction should also be considered, even when standard laboratory values are within normal range. Although most cases of hypothyroidism will respond well to the use of hormone replacement medication, such as Synthroid (Abbott Laboratories, Abbott Park, Ill), levothyroxine sodium, or Levoxyl (King Pharmaceuticals Research & Development, Bristol, Tenn). However, these medications only contain L-thyroxine (T4). In patients who have T4 to T3 conversion disorders (also known as euthyroid sick syndrome, low T3 syndrome), possibly secondary to a long-term stress disorder, they often do not feel relief of their symptoms when placed on T4

therapy alone. The use of a combination of thyroxine (T4) and triiodothyronine (T3) therapy (eg, Cytomel [Jones Pharma, St. Louis, Mo]) is gaining popularity with many physicians attempting to manage patients refractive to T4 therapy alone. These patients may not have overt abnormalities on standard thyroid laboratory studies and the clinician may need to pay close attention to patient symptomology in the diagnosis of these variants of thyroid dysfunction.

It is often important to evaluate adrenal status in the chronically fatigued patient because increases in catecholamines and upregulation of the sympathetic nervous system have been implicated in FMS, as previously discussed. Morning serum cortisol and urinary catecholamine metabolites can be beneficial in assessing adrenal dysfunction, including the low cortisol and elevated catecholamine pattern of posttraumatic stress disorder. In patients with this pattern, psychologic counseling and stress-reducing lifestyle modifications are imperative.

In summary, there appear to be a certain subset of patients who may receive an inappropriate diagnosis of FMS and do not display the entire spectrum of clinical elements indicative of classic FMS, do not show any positive laboratory findings indicative of overt organic pathology or disease, yet have significant functional deficits in certain organ systems. The functional approach to the treatment of these patients is not centered around any one agent or modality as the curative, or even palliative, solution. Treatment is centered on the principle that restoration of proper cellular metabolism, through balancing the endocrine system, the repletion of nutritional deficiencies, and the reduction of cumulative toxic load and oxidative stress will allow normalization of mitochondrial respiration, cellular energy production, and ultimately to a reduction in the signs and symptoms of low energy, fatigue, and widespread achiness. Many of these factors can be addressed by simple lifestyle changes by the patient, including eating a fresh-food varied and balanced diet, consuming reasonable vitamin and mineral supplementation, and engaging in stress management techniques such as regular light exercise, proper sleep, adequate recreation and relaxation, deep-breathing exercises, yoga, meditation, prayer, etc.

## Musculoskeletal Disorders Misdiagnosed as FMS

Patients with FMS present with widespread pain in multiple body regions. In addition, the character and distribution of this widespread pain are typically poorly described by the patient as vague and diffuse. This presents a diagnostic conundrum because of generally poor knowledge about musculoskeletal disorders within primary care medicine[23] and the fact that standard internal medicine textbooks (eg, Cecil's or Harrison's) present a limited subset of potential etiologies and, thus, diagnoses for these kinds of pains. Symptoms that do not follow dermatome or radicular pain distributions, or commonly known visceral referred pain patterns, could easily be misdiagnosed as "widespread pain," leading to a misdiagnosis of FMS. However, there are well-documented pain generators in the musculoskeletal tissues that are not typically recognized by clinicians whose training is more focused on visceral referred pain patterns.

As early as the 1930s, Kellgren[24] showed that deep somatic tissues (ligaments, muscles, and periosteum) exposed to hypertonic saline injection produce unusual referred pain distributions often at a sizeable distance from the injection site. Bogduk et al[25,26] have provided compelling evidence that it is common for patients to present with pains of unusual, but predictable and reproducible, distribution that clearly emanate from spinal facet and sacroiliac joints, which are distinct from radicular pain. Their elegant studies used anesthetic joint blocks to confirm that the facet and sacroiliac joints were in fact the source of many patients' pain.[25,26]

Unfortunately, the diagnosis of facet and sacroiliac joint pain is not a simple matter. Radiologic studies, MRI and computerized tomography scans, and bone scan have little diagnostic yield because there is not necessarily any pathoanatomic changes in these joints associated with the referred pain patterns. Unusual patterns of back or neck pain coupled with negative diagnostic imaging studies might lead the unwary clinician to declare FMS as the diagnosis, when in fact the pain is emanating from the facet or sacroiliac joints.

Even the well-known classic presentation of spinal disk herniation with neck/back pain and radicular pain into the upper/lower extremities is not as simple to diagnose as once thought. This "classic presentation" of disk herniation is actually rather uncommon. Studies have shown that internal disk derangements and/or annular tears without frank herniation are common and do not cause dermatome pain. These cases of discogenic pain can manifest as symptoms of buttock or thigh pain, even pain in the lower leg, without any true irritation of the existing nerve roots.[27] Using the presence of pain distal to the knee to rule-in radicular pain rather than discogenic referred pain is untenable given the fact that internal disk derangement alone can result in distal leg pain. It is also possible that false-negative MRI results can occur, in which the patient truly has a serious disk derangement but the MRI fails to image the protrusion adequately.[28] Therefore, the unexplained presence of odd or unusual pain in the distal extremities could cause a physician to erroneously believe that the pain might not be emanating from a disk and instead choose FMS as the diagnosis.

Lastly, one of the most common causes of unusual referred pain in the torso and extremities is the phenomenon of myofascial referred pain. Myofascial trigger points (TrP) have been documented as a common clinically

important cause of referred pain, also of atypical character and distribution.[29] Trigger points are often found in the muscles of the upper extremity, shoulder, and posterior neck, and cause unusual referred pain patterns into the head, face, and upper extremity.[30] These TrPs palpate as tender nodules in an area of taut bands of skeletal muscle and represent some unknown type of focal muscle dysfunction. Trigger points may easily be mistaken for the tender points (TeP) found in FMS. Clearly, the TePs found in FMS are not areas of muscle dysfunction but rather areas of cutaneous tenderness that are thought to be peripheral hyperalgesia zones because of central sensitization. Tender points do not have any palpable tissue texture change and are not associated with taut bands of skeletal muscle. The inability of physicians to differentiate between the TrPs of myofascial pain and the TePs found in FMS may lead to an overdiagnosis of FMS.[31]

## Conclusion

It is proposed in this article that there is a problem with the current conceptual model of FMS as one grandiose syndrome into which all patients with unexplained widespread pain are categorized. Emerging evidence suggests that there is also a disturbing trend toward overdiagnosis of FMS within primary care medicine, and that many other disorders may mimic the symptoms of FMS. There is clearly a "classic" presentation of FMS in which pronounced widespread allodynia is the hallmark symptom, with a number of other associated symptoms suggestive of neuroendocrine dysfunction. In these cases of classic FMS, the patient likely is experiencing a psychosomatic disorder in which the physical symptoms are manifestations of prolonged limbic system activation that causes central sensitization and a wide variety of neuroendocrine disturbances. These patients clearly need a psychosocial approach to the management of their physical symptoms, which are quite real, but secondary to their comorbid mental illness.

The relevance for clinicians who see these patients is the recognition that mental illness and mood disorders may be the root cause of the symptom cluster known as FMS. If it is true that this subset of patients is exhibiting a psychosomatic illness, it would explain the relatively poor results of most current treatment programs, which emphasize the musculoskeletal system as the source of pain. It would seem more appropriate for the clinician to refer these patients for cognitive behavioral therapy or other forms of psychologic counseling, in addition to physical therapy, massage, or chiropractic treatment. A recent systematic review of the FMS literature has shown that cognitive behavioral therapy is an effective treatment strategy for patients with FMS, along with mild exercise and low dose antidepressant medication.[8]

However, a large number of patients clearly do not present with a history and symptoms suggestive of classic FMS. They present with "widespread pain," yet they do not have true widespread allodynia. Furthermore, they do not complain of any associated sleep disorder, cognitive deficit, sympathetic or parasympathetic functional disorders, or the other symptoms associated with classic FMS. These patients require a complete medical examination and appropriate laboratory screening tests to rule out any number of diseases or conditions that could be the root cause of their vague symptoms of unusual pain. When all standard medical tests are negative, and the clinician is relatively certain no underlying pathology exists, it may be appropriate to have the patient screened for functional or metabolic dysfunction. This often requires an examination with a complementary medicine clinician such as a physician with additional training in functional or metabolic medicine, naturopathic physician, nutritionist, or other clinicians with such training.

Lastly, many common musculoskeletal conditions can mimic FMS. It is imperative that the clinician understand the many musculoskeletal sources of unusual referred pain patterns that could be misdiagnosed as FMS. A careful physical examination by a clinician with experience in musculoskeletal differential diagnosis would help to sort out more of these cases, which could potentially reduce the error rate of FMS misdiagnosis. Collaborative patient management between clinicians, chiropractors, osteopaths, and physical therapists would seem to be the best way to ensure that patients with these musculoskeletal causes of widespread pain would receive the appropriate diagnosis and therapy, without resorting to a default diagnosis of FMS in all cases of widespread pain.

The diagnostic algorithm (Appendix A) is presented as a quick reference for the clinician to sort through all of the above possibilities when confronting the diagnostic challenge of a patient with multiple physical complaints and widespread pain. It is suggested that the diagnosis of FMS be reserved for certain patients who fit the "classic" presentation of the disorder, and that the 3 other categories be considered carefully before defaulting to an FMS diagnosis. We must emphasize that our proposed 4 subsets are merely a hypothesis and not based upon any data from clinical trials. Future research that explores the various etiologies of the symptom complex presently called *FMS* may very well lead to abandonment of the term FMS, as the various causes of these symptoms unfold.

Many patients may be given the label "fibromyalgia" too quickly, when they may indeed have one or more of these other conditions as the cause of their symptoms. Clinicians are urged to carefully evaluate all patients with widespread pain and fatigue to find the root cause of their symptoms, rather than default to the vague diagnosis of "fibromyalgia" which may not actually be any single disease process but a variable symptom complex with

several etiologies. This article concludes with the presentation of a diagnostic algorithm that is suggested as an aide for the differential diagnosis of patients with chronic widespread pain.

**Practical Applications**

- The diagnosis of fibromyalgia syndrome should not be used to categorize all patients with widespread and fatigue of unknown etiology.
- This article suggests that there are at least 4 distinct subsets of patients with widespread pain; each of which requires a distinct treatment approach.
- Many other medical conditions can be misdiagnosed as fibromyalgia syndrome, including hypothyroidism, anemia, Lyme disease, dysglycemias, metabolic dysfunction, myofascial pain, and other musculoskeletal disorders.

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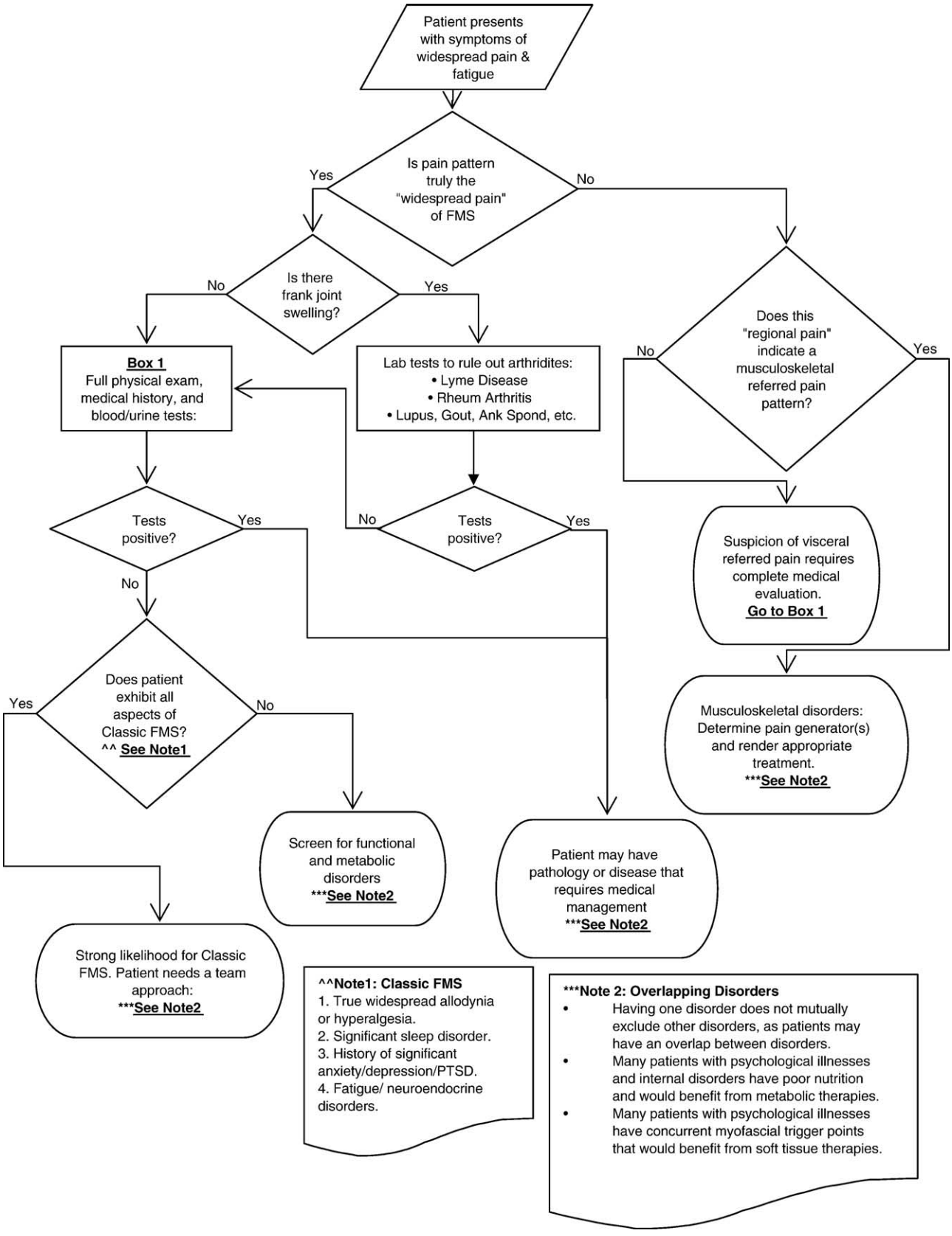
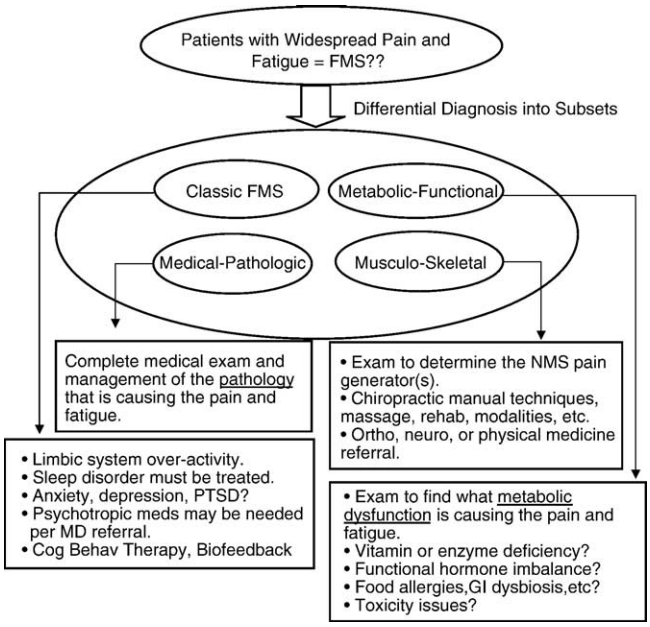
## APPENDIX A


Patient presents with symptoms of widespread pain & fatigue
Is pain pattern truly the "widespread pain" of FMS
Yes
No
Is there frank joint swelling?
No
Yes
Box 1
Full physical exam, medical history, and blood/urine tests:
Lab tests to rule out arthridites:
• Lyme Disease
• Rheum Arthritis
• Lupus, Gout, Ank Spond, etc.
Does this "regional pain" indicate a musculoskeletal referred pain pattern?
No
Yes
Tests positive?
Yes
No
Tests positive?
No
Yes
Suspicion of visceral referred pain requires complete medical evaluation.
Go to Box 1
Does patient exhibit all aspects of Classic FMS?
^^ See Note1
Yes
No
Musculoskeletal disorders: Determine pain generator(s) and render appropriate treatment.
***See Note2
Screen for functional and metabolic disorders
***See Note2
Patient may have pathology or disease that requires medical management
***See Note2
Strong likelihood for Classic FMS. Patient needs a team approach:
***See Note2
^^Note1: Classic FMS
1. True widespread allodynia or hyperalgesia.
2. Significant sleep disorder.
3. History of significant anxiety/depression/PTSD.
4. Fatigue/ neuroendocrine disorders.
***Note 2: Overlapping Disorders
• Having one disorder does not mutually exclude other disorders, as patients may have an overlap between disorders.
• Many patients with psychological illnesses and internal disorders have poor nutrition and would benefit from metabolic therapies.
• Many patients with psychological illnesses have concurrent myofascial trigger points that would benefit from soft tissue therapies.

## Appendix B


Patients with Widespread Pain and Fatigue = FMS??
Differential Diagnosis into Subsets
Classic FMS
Metabolic-Functional
Medical-Pathologic
Musculo-Skeletal
Complete medical exam and management of the pathology that is causing the pain and fatigue.
• Exam to determine the NMS pain generator(s).
• Chiropractic manual techniques, massage, rehab, modalities, etc.
• Ortho, neuro, or physical medicine referral.
• Limbic system over-activity.
• Sleep disorder must be treated.
• Anxiety, depression, PTSD?
• Psychotropic meds may be needed per MD referral.
• Cog Behav Therapy, Biofeedback
• Exam to find what metabolic dysfunction is causing the pain and fatigue.
• Vitamin or enzyme deficiency?
• Functional hormone imbalance?
• Food allergies,GI dysbiosis,etc?
• Toxicity issues?