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Differential Diagnosis of CFS/CFIDS/ME and Fibromyalgia

Fibromyalgia (FM) means "soft tissue and muscle pain". The soft tissues are tendons and ligaments. It is a chronic pain syndrome often associated with the Chronic Fatigue Syndrome/Chronic Fatigue and Immune Dysfunction Syndrome/Myalgic Encephalopathy (CFS/CFIDS/ME) and sometimes confused with it. The pain can be severe enough to interfere with routine daily activities. It migrates, can be achy, throbbing, shooting, or stabbing, and is worse in areas used most, like the neck or back. FM is associated with "tender points" which are painful when pressure is applied to them. Individuals often say they awaken feeling as if they hadn't slept. A sudden onset of profound fatigue can occur during or following exertion. Many other symptoms are common to fibromyalgia, including stiffness on waking, memory and concentration problems, excessive sensitivity of the senses, headaches, Temporomandibular Joint Syndrome (TMJ), irritable bowel, and bladder and muscle spasm.

Fibrositis, an older name, is still used interchangeably with fibromyalgia.

Research authorities vary in viewpoint as to the relation of FM and CFS/CFIDS/ME, but the best research to date indicates that the two illnesses, while often associated, are different and separable—both in nature of causation and in their pathophysiologies (effects on processes in the body.) The fact that the two illnesses are the province of separate specialties can also lead to diagnostic problems. As a rheumatologist is trained in rheumatological illnesses, there are occurrences of CFS/CFIDS/ME being diagnosed as FM when the physician is not well versed in CFS/CFIDS/ME diagnosis. And an infectious disease specialist may be prone to misdiagnosing FM as CFS/CFIDS/ME. Therefore, when there is doubt about which illness a patient has, s/he should become familiar with the differences between the two illnesses and seek a physician

who knows how to diagnose both illnesses.

Diagnosis of Fibromyalgia (FM)

The 1990 U.S. College of Rheumatology diagnostic criteria are straightforward:

1. Widespread pain for at least 3 months.
2. Pain in all four quadrants of the body: right side, left side, above and below the waist.
3. Pain in at least 11 of 18 specified tender points when they are pressed. These 18 sites cluster around the neck, shoulder, chest, hip, knee, and elbow regions.

No exclusions are made for the presence of concomitant radiographic or laboratory abnormalities.

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Differential Diagnosis of CFIDS and Multiple Sclerosis

A percentage of CFS/CFIDS/ME patients, either recently diagnosed or who have been ill for a substantially longer period, have neurological signs and symptoms. Drs. Anthony Komaroff and Dedra Buchwald reported seeing ataxia (difficulty with muscle coordination), focal weakness, and transient blindness in CFS/CFIDS/ME patients. Drs. Henderson and Shelokov, in their study of CFS-like outbreaks in the U.S., found signs of paresis (partial paralysis), facial paresis, urinary retention, diplopia (double vision) and Babinski's sign (improper nerve conduction in the toes.)

Multiple Sclerosis (MS) is a neurological illness in which the myelin sheath covering of nerves is progressively destroyed. According to the National Multiple Sclerosis Society this degenerative process "impairs the transmission of nerve impulses to muscles and other organs of the body. The symptoms of MS include weakness numbness, tremor, loss of vision, pain, paralysis, loss of balance and bowel dysfunction."

There is at least the distinct appearance of overlap in some of the neurological signs and symptoms between CFS/CFIDS/ME and MS. A leading international expert in MS, Dr. Charles

Poser, has also studied CFS/CFIDS/ME. In an article entitled "The Differential Diagnosis of CFS and MS" published in the *CFIDS Research Review* (CFIDS Association of America), Dr. Poser writes: "An alarming number of CFS patients are misdiagnosed with multiple sclerosis (MS). The severity and symptoms of CFS fluctuate and sometimes mimic the relapses and remission of MS...In a review of 366 patients referred to me who had been diagnosed with MS by a board-certified neurologist, only 236 patients (65%) had been correctly diagnosed. An astounding 28 (22%) actually had CFS."

The differential diagnosis between the two illnesses can be complicated, even to a neurologist. For Dr. Poser's comprehensive guidelines for making the differential diagnosis please see his complete article listed under *More Resources*.

In summary, his basic points are as follows: most patients who have definite neurological symptoms that suggest MS are referred to a neurologist who will routinely order an MRI. Many patients with CFS/CFIDS/ME will show punctate white spots in the white matter—as will MS patients. However the definition and areas of the spots are somewhat different in the two illnesses, and some radiologists may miss these distinctions. Dr. Poser is firm that MS must not be diagnosed on the basis of MRIs alone. He states that while many CFS/CFIDS/ME signs and symptoms mimic those of MS, there are significant differences, which thereby demand a full and careful evaluation and history. MS rarely shows the infectious-like symptoms of CFS/CFIDS/ME, nor the broader multiplicity of symptoms across physiological systems of CFS/CFIDS/ME.

To further complicate matters, MS especially in its initial stages, can more closely mimic CFS/CFIDS/ME symptoms. Numbers of patients have, as time progressed, been diagnosed as having one illness and then the other. It is absolutely important that a patient suspected of having CFS, but having clear neurological symptoms, be referred to a neurologist qualified to make the differential diagnosis. We suggest all patients with clear neurological symptoms provide a copy of Dr. Poser's article to their doctor(s).

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Differential Diagnosis of CFS/CFIDS/ME and Chronic Lyme Disease

Currently the differential diagnosis between CFS/CFIDS/ME and Chronic Lyme disease is both

difficult and under dispute. One reason is because of conflicting opinions among Lyme Disease specialists as to the actual case definition of Lyme disease and its proper and accurate diagnosis. Some Lyme disease specialists deny that chronic Lyme Disease exists at all. So they claim that Lyme Disease, properly treated, does not have a chronic form (more than a few months duration.). In fact, there is no doubt that chronic Lyme disease is a very real illness. Some physicians who acknowledge this also often theorize that any possible chronic Lyme is really CFS/CFIDS/ME.

The major symptoms of chronic Lyme disease that overlap with CFS/CFIDS/ME are:

- cognitive dysfunction and mood changes
- central nervous system irritability, including parathesias (numbness, tingling crawling and itching sensations)
- fatigue
- flu-like illness: fevers, malaise, headache, muscle aches
- joint aches (arthralgia) and intermittent swelling and pain of one or a few joints.
- sleep disturbance

Differential diagnosis between CFS/CFIDS/ME and chronic Lyme is of critical importance. Chronic Lyme disease left untreated can become extremely serious, even life-threatening. The longer it is left untreated, the longer antibiotic treatment may take to work effectively. Therefore, misdiagnosis of chronic Lyme disease as CFS/CFIDS/ME can have severe consequences for patients.

What are some of the issues of differential diagnosis? First, Lyme disease must be diagnosed properly—and there is much dispute as to how such diagnosis is properly done. The *Centers for Disease Control Protocol*, which most doctors will follow, is seriously deficient. The protocol first calls for an Elisa test, which if positive, is followed by the more accurate Western Blot test. However, the Elisa test may show up to 80% false negatives—meaning the person is actually positive for Lyme, but the test comes up negative. Therefore, anyone with chronic Lyme symptoms should have the Western Blot immediately. However there is much dispute and confusion among specialists about the proper interpretation of the Western Blot. The Western Blot is not an "all or nothing" test. There are numerous bands which must be looked at and interpreted. A non-specialist may read a Western blot as negative, when a knowledgeable specialist may see a likelihood of Lyme in the same test.

Other specialized laboratory tests, which may provide greater diagnostic information, can also be run by specialists. Further accurate diagnosis involves careful clinical evaluation and detailed history.

A patient suspected of having chronic Lyme disease and his/her family must educate themselves about how chronic Lyme is diagnosed and where to find a doctor who has the knowledge and motivation to make the most accurate diagnosis possible.

Complicating the matter is that some Lyme specialists will over diagnose chronic Lyme and will make a tentative diagnosis, after testing, primarily on symptoms and history. Some physicians will begin treatment as an adjunct to diagnosis, the notion being that if the treatment begins to work, then the Chronic Lyme is identified.

The serious issue here is that CFS/CFIDS/ME and Chronic Lyme may clinically appear almost identical. If a CFS/CFIDS/ME patient is misdiagnosed with Chronic Lyme and started on treatment, there can be severe consequences, both from the effects of treatment and the time and costs involved.

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Differential Diagnosis of CFS/CFIDS/ME and Chiari Malformation

Around the year 2000, there was significant interest in whether some cases of CFS/CFIDS/ME were in caused by Chiari Malformation—an anatomical condition in which a portion of the brain is squeezed too tightly into the top of the spinal canal; or alternatively the upper portion of the spinal cord is squeezed into a spinal canal that is too narrow. Some specialists diagnosed this condition in persons exhibiting CFS/CFIDS/ME symptoms. These physicians carried out surgeries to correct the Chiari malformation. Some patients improved, others did not. A number of CFS/CFIDS/ME specialists were greatly concerned about the Chiari malformation diagnosis and subsequent surgery. For more information on this differential diagnosis, please see Voelker, "Chiari Conundrum: Researchers Tackle a Brain Puzzle for the 21st Century," *JAMA* 301(2) (2009): 147-149.

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Differential Diagnosis Between CFS/CFIDS/ME and Psychiatric Disorders

Unfortunately, the issue of differential diagnosis between CFS/CFIDS/ME and psychiatric illnesses is not simply a straightforward one based on clinical history and medical evaluation. Since the illness first became publicly known in the late 1980s, there has been a wide gap in the developing understanding of CFS/CFIDS/ME between the many independent clinicians and researchers directly involved with treating patients and conducting careful and rigorous research, and the U.S. government public health and research agencies and a minority of physicians and researchers.

Beginning in the late 1980s, primary care physicians and specialists began to encounter patients with a severe flu-like illness, often with neurological and other symptoms, that was not resolving in a few weeks or months. In many patients this illness became chronic over a period of years. Although researchers were able to find abnormalities in the immune systems of patients and punctuate lesions on MRI, routine laboratory tests often showed few abnormalities. Despite multiple research efforts, no clear cause could be found, although many of the more serious researchers suspected a viral link, since antibodies to a number of viruses were found to be elevated.

The Centers for Disease Control & Prevention (CDC) almost immediately told physicians, patients and the public that the illness was substantially psychiatric in nature—"atypical depression", neurasthenia, somatization disorder, a pathological response to stress, or poor coping behavior. It came to be called "yuppie flu"—referring to young well-educated people who supposedly had nothing serious with which to occupy themselves. Articles by government and other scientists discussed the sickness of the "overachiever".

Hence the question was not one of scientific differential diagnosis, but became instead a medical and political debate as to whether CFS/CFIDS/ME was psychiatric or a physical illness (such as mononucleosis or multiple sclerosis).

Government and other scientists, on the basis of poorly designed research were portraying the illness in the press and medical circles as psychiatric and not a real physical illness. Treatment would consist of psychiatric medication and learning to more effectively solve problems. The press and media generally communicated this point of view to the public. Patients who were demonstrably and seriously ill were facing doubt and questions about whether their illness was

"real". Some physicians were telling patients "there is nothing wrong with you", "it's all in your head", "just get some rest and you'll be fine". It's an unfortunate fact of medicine that when some physicians cannot find clear abnormalities on laboratory and other medical tests, their conclusion will be that "nothing is wrong"—even when the conclusion is at variance with the patient's obvious condition. Some physicians may not admit that they can't understand what's wrong and simply say: "You are clearly ill, but I can't figure out what you have." For some it's easier to be able to say something certain like "there's nothing wrong", rather to admit to a more evidence-based uncertainty.

For most of the 1990s, public health and research agencies, despite developing research findings to the contrary, portrayed and labeled the illness as substantially psychiatric. This viewpoint filtered down to physicians. However, as research progressed throughout the 1990s and into the present decade, more and more evidence mounted that the illness was physiological and multi-systemic in nature. Therefore, it is now possible, using proper and careful diagnostic techniques, to make an accurate differential diagnosis between CFS and psychiatric illnesses. This is not to say that CFS can't co-exist with anxiety or depression—more often of secondary nature.

Summary of Some Research Separating Psychiatric Illness from CFS/CFIDS/ME

Excerpt from: Anthony Komaroff, M.D., "A 56-Year Old Woman with Chronic Fatigue Syndrome", *The American Journal of Medicine* (1997)October 8.

Differences between CFS and Major Depression: "Although fatigue and some of the other symptoms of CFS could reflect a primary psychiatric disorder, several other symptoms of CFS are not characteristic of psychiatric illnesses: for example, sore throat, adenopathy, and post-exertion malaise..."

"...a careful controlled trial failed to demonstrate an improvement in fatigue from treatment with fluoxetine in patients with CFS, even in those with a concomitant major depression. Indeed, even the concomitant depression did not improve, indicating that the phenotype called 'depression' in CFS patients may stem from an unusual underlying pathology.

"...studies using structured psychiatric interviews find no evidence of major depression in many (25-60%) of patients with CFS, either before or after the onset of CFS. In our studies, the majority of patients also have no evidence of anxiety disorders at any time in their lives, including after the onset of CFS."

A study by MacDonald *et al.* in the *American Journal of Medicine*, May 1996, found that CFS patients were not more depressed than controls prior to illness onset.

In the Summer/Fall 1988 *CFIDS Chronicle*, Dr. Komaroff responded to Dr. Strauss' paper, "Lifetime of Mental Illness in People with CFS." Strauss's paper indicated 7.1% of CFS patients had histories of major depression. Dr. Komaroff pointed out that in the population-at-large, a history of major depression is present at a rate of 6.9%.

In *Osler's Web*, Hillary Johnson reports a study done by Dr. Komaroff in Boston of patients suffering from CFS-like symptoms, including recurrent swollen lymph nodes, joint pain, parathesias, difficulty sleeping, severe myalgias, headaches and severe fatigue for at least six months. "Komaroff's team found no incidence of psychiatric or other chronic diagnoses in the history of the patients."

The *CFIDS Chronicle* in September 1997 reported on a study done by Jorge and Goodnick, "Chronic Fatigue Syndrome and Depression; Biological Differentiation and Treatment," in *Psychiatric Annals*, May 1997: "...[They] distinguish CFIDS from depression in terms of physical signs and symptoms, sleep, fatigue, memory, biological parameters, brain imaging, immunology and treatment. They identify differences between the two conditions based on an extensive review of the literature."

Hilary Johnson, in *Osler's Web* also recounts that the CDC itself found, in 1990, that 2/3 of patients being referred to the Agency's surveillance project "...were free of psychological problems when their disease began." She quotes Walter Gunn, M.D. at the CDC (1990): "The majority (who meet the case definition of CFS) did not have a psychological problem concurrent with the onset of fatigue. So for anyone who says that this is depression in disguise, we can say, 'That is not what the data says.' We're not seeing any rate of depression higher than the normal population." Gunn further explained, "...the psychological profiles of CFS patients resembled those of people suffering from multiple sclerosis and other chronic illnesses."

Differential Diagnosis Between CFS/CFIDS/ME and Major Depression

Under DSM-IV a person must have 5 or more of the qualifying symptoms to be diagnosed with major depression. Of these symptoms, only 3: fatigue or loss of energy every day, diminished

ability to think or concentrate, and insomnia or hypersomnia nearly everyday, directly overlap with the 7 CFS diagnostic symptoms of the 1994 CDC Definition of CFS. Since to obtain a CFS diagnosis a patient must have at least 4 of 7 qualifying symptoms, a CFS patient would not normally also be diagnosed as having major depression. Clearly at variance with the 9 diagnostic symptoms of depression are the following CFS diagnostic symptoms: post-exertional malaise (worsening of symptoms after exertion, even up to a day or two later); headaches of a new type or severity; muscle pain; and the infectious-type symptoms very uncharacteristic of depression such as sore throat; and tender lymph nodes in the neck or underarm area. If mild fever or chills and non-exudative pharyngitis from the 1988 definition are added, the gap between the two illnesses is widened.

From the Massachusetts CFIDS/ME & FM Association *Physicians Primer* which was written by medical professionals: "The depression commonly seen with CFIDS may resemble a major depression with atypical features. [Secondary depression in CFIDS is similar to secondary depression in other patients with chronic physical illnesses.] Both may include sleep disorder but in CFIDS, the sleep disorder involves non-REM sleep disturbances instead of the REM sleep disturbances seen in major depression. Although fatigue is present in both conditions, the fatigue in CFIDS is profound and accompanied by intense frustration from not being able to do what one still wants to do; i.e.,

patients do not usually lose motivation and interest

. In contrast, apathy and anhedonia generally accompany the fatigue in primary depression. Furthermore, persons suffering from a severe primary depression may 'forget' that they have ever felt any other way and may have given up hope that their bleak state can improve. Patients with CFIDS, on the other hand, are exquisitely aware of not feeling as well as they used to or as well as they hope to.

"Patients with depression and anxiety often complain of difficulty with thinking and concentration, as do patients with CFIDS; however, the manifestations of cognitive abnormalities on neuropsychological testing typically reveal different patterns. CFIDS patients tend to present a characteristic profile of apparently multi-focal deficits including short-term memory, figure-ground, and aphasic difficulties. Furthermore, CFIDS sufferers may benefit from very low doses of antidepressant medication and may be unable to tolerate the usual therapeutic dose. And finally, a concurrent major depression in CFIDS may respond to antidepressant medication, but the systemic complaints and cognitive impairments persist even when mood improves, thus differentiating CFIDS from an atypical depression or 'depressive equivalent'."

A major study by Strauss and Demitrack found that patients with major depression have an excess of cortisol. Also according to the study, patients with CFS/CFIDS/ME were found to have low cortisol levels.

Finally, a major distinction is that when patients with depression actually get up and exert themselves, they often feel better and do not suffer major post-exertional illness. This is untrue with CFS/CFIDS/ME patients.

Differential Diagnosis Between CFS/CFIDS/ME and Generalized Anxiety Disorder (DSM-IV 300.02)

Both the 1994 CFS criteria and the DSM-IV criteria for Generalized Anxiety Disorder have in common a requirement of fatigue of at least 6 months duration. Each criteria also have in common certain neuropsychological symptoms—however with important distinctions. Sleep disturbance occurs in both illnesses, with specific differential characteristics.

However, the 1994 CFS definition requires at least one more symptom for diagnosis, none of which match further symptoms diagnostic of Anxiety disorder. Further symptoms for CFS include post-exertional malaise, muscle pain, and the infectious-like symptoms—all of which are not diagnostic of anxiety. Of course, CFS/CFIDS/ME patients may have secondary anxiety and worry because they are chronically physically ill.

From the Massachusetts CFIDS/ME & FM Association *Physician's Primer* by medical professionals: "As in anxiety disorder, CFIDS patients may report symptoms of autonomic hyperactivity, motor tension, worry and/or dread, dizziness, loss of balance, lightheadedness, or hypersensitivity. Panic attacks or feeling overwhelmed may even be a patient's presenting complaint, but a careful history will reveal other characteristic multi-systemic symptoms of the illness."

Differential Diagnosis Between CFS/CFIDS/ME and Somatoform Disorders

There are a number of somatoform disorders. The most relevant, in terms of differential diagnosis with CFS/CFID/MES, are somatization disorder and "neurasthenia".

The DSM-IV criteria for *somatization disorder* require a history of many physical complaints beginning before the age of 30. Epidemiological research on CFS/CFIDS/ME demonstrates that the majority of CFIDS patients have an onset at an age above 30. "The onset of multiple physical symptoms later in life is almost always due to physical disease." (Massachusetts CFIDS/ME & FM Association *Physician's Primer*). Fatigue, which is a major CFS/CFIDS/ME symptom is not a symptom of somatization disorder;

nor is disordered sleep or decreased concentration. The only symptoms in common are head, joint, and possible muscle pain.

Neurasthenia, characterized by fatigue and weakness, is listed in DSM-IV as *Undifferentiated Somatoform Disorder*

. Neurasthenia, a common diagnosis at the end of the 19th

century has generally fallen into disfavor. The DSM-IV definition is: "one or more physical complaints (e.g., fatigue, loss of appetite, gastrointestinal, or urinary complaints) for which either 1) the symptoms cannot be fully explained by a known general medical condition, or 2) when there is a medical condition, the physical complaints are excessive in relation to the condition."

The definition of "neurasthenia" is obviously vague—it requires an interpretation that physical symptoms are either "excessive" or "unexplained". Specialists familiar with the symptomatology, pathophysiology, epidemiology, and the extensive research into metabolic dysregulation in CFS/CFIDS/ME would not be prone to making the psychiatric diagnosis.

Differential Diagnosis Between CFS/CFIDS/ME and Phobic Avoidance Disorders

(From the Massachusetts CFIDS/ME & FM Association *Physician's Primer* by medical professionals): "It is important to differentiate CFIDS from phobic avoidance disorders. Unlike agoraphobia, staying home does not significantly alleviate the patient's symptoms. In children, school phobia must also be considered but can usually be ruled out by the persistence of the symptoms on weekends and holidays and by a lack of premorbid history suggestive of the common patterns for school avoidance."

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Differential Diagnosis between CFS/CFIDS/ME and Multiple Chemical Sensitivities (MCS)

Please see the article [CFIDS and Multiple Chemical Sensitivity \(MCS \): What's The Connection](#)

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More Resources

[A Personal Journey Into Lyme Disease](#)

[Cardiac Symptoms and Abnormalities Documented in CFS Patients: \(A summary of 4 studies by Lerner et al.\)](#)

[CFIDS and Multiple Chemical Sensitivity \(MCS \): What's The Connection?](#)

[CFIDS/FM and Chiari Malformation Surgery](#)

[Dr. Sam Donta: The Interface of Chronic Lyme Disease, CFS and FM](#)

[Lyme Disease and its Symptoms](#)

[National Multiple Sclerosis Society](#)

[The Differential Diagnosis of CFS and MS](#) by Charles M. Poser, M.D., FRCP (GLE), 2000

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