APPENDIX 4. Signs and Symptoms

As the neurological, immune and endocrine systems are widely distributed, symptoms are numerous, multiform and of variable intensities. Many of the following symptoms are not present in everyone or at all times and, therefore, cannot be included as part of the criteria for diagnosis.

Circulatory System

____ neurally mediated hypotension (NMH)
____ postural orthostatic tachycardia syndrome
____ delayed orthostatic hypotension
____ light-headedness
____ palpitations
____ fluid retention
____ extreme palor
____ bruising

Digestive System

____ lump in throat
____ nausea
____ heart burn
____ abdominal pain
____ irritable bowel syndrome

Neuroendocrine System

____ loss of thermostatic stability–subnormal body temperature or diurnal fluctuations
____ hot flushes
____ excessive sweating or night sweats
____ feelings of feverishness
____ feelings of cold extremities
____ heat/cold intolerance
____ anorexia or abnormal appetite
____ marked weight change
____ hair loss

Musculoskeletal System

____ myalgia
____ muscle cramps, particularly in legs
____ chest pressure and pain
____ arthralgia
____ TMJ

Nervous System

____ persistent fatigue
____ lack of endurance
____ migraines or new onset headaches
____ seizure like phenomena

Sensory

____ hypersensitivity to pain
____ hyper-responsiveness to noxious stimuli
____ perceptual & dimensional distortions
____ feeling of burning or swelling
____ overload phenomena
____ loss of cognitive map
____ altered taste and/or smell

Cognitive

____ difficulties processing information
____ concentration problems
____ confusion
____ difficulties with word retrieval
____ word mix-ups
____ short-term memory difficulties
____ slowness in cognitive processes

Motor and Balance

____ muscle weakness or paralysis
____ poor balance, ataxia & tandem gait
____ clumsiness & tendency to drop things
____ difficulty in tandem gait
____ atypical numbness or tingling

Sleep Disturbances

____ sleep disturbance–hyper- or insomnia
____ non-refreshing sleep

Visual and Auditory Disturbances

____ photophobia
____ visual changes or eye pain
____ double, blurred or wavy vision
____ dry or itchy eyes
____ tinnitus–buzzing or ringing in ears
____ hyperacusis & cocktail party phenomena

Neuropsychological

____ loss of adaptability
____ worsening of symptoms with stress
____ emotional flattening or personality change
____ anxiety &/or panic attacks
____ reactive depression

Immune System

____ tender lymph nodes
____ recurrent sore throat
____ recurrent flu-like symptoms
____ new sensitivities to medications, chemicals

Reproductive System

____ dysmenorrhea
____ PMS or irregular menstrual cycles
____ loss of sexual libido or impotence

Respiratory System

____ exertional dyspnea
____ sinusitis
____ persistent cough & wheezing

Urinary System

____ urinary frequency, bladder dysfunction

APPENDIX 5. ME/CFS Clinical Diagnstic Worksheet

NAME **DATE**

☐ 1. **Fatigue:** Patient must have a significant degree of new onset, unexplained, persistent or recurrent physical and mental fatigue that substantially reduces activity level.

☐ 2. **Post-Exertional Malaise and Fatigue:** There is an inappropriate loss of physical and mental stamina, rapid muscular and cognitive fatigability, post-exertional fatigue and/or malaise and/or pain and a tendency for other associated symptoms within the patient's cluster to worsen. There is a pathological slow recovery period–usually 24 hours or longer.

☐ 3. **Sleep Dysfunction:*** There is unrefreshed sleep or sleep quantity or rhythm disturbance such as reversed or chaotic diurnal sleep rhythm.

☐ 4. **Pain:*** There is a significant degree of myalgia. Pain can be experienced in the muscles and joints and is often migratory in nature. Often there are significant **headaches** of new type, pattern or severity.

☐ 5. **Neurological/Cognitive Manifestations:** Two or more of the following difficulties should be present: confusion, impairment of concentration and short-term memory consolidation, disorientation, difficulty with information processing, categorizing and word retrieval, and perceptual and sensory disturbances–e.g., spatial instability, and inability to focus vision. Ataxia, muscle weakness and fasciculations are common. There may be overload phenomena: cognitive, sensory–e.g., photophobia and hypersensitivity to noise–and/or emotional overload, which may lead to "crash"[1] periods and/or anxiety.

☐ 6. **At Least One Symptom from Two of the Following Categories:**

____ **Autonomic Manifestations:** orthostatic intolerance–NMH, POTS, delayed postural hypotension, vertigo; light-headedness, extreme pallor; nausea and IBS; urinary frequency and bladder dysfunction; palpitations with or without cardiac arrhythmia; palpitations, and exertional dyspnea.

____ **Neuroendocrine Manifestations:** loss of thermostatic stability–subnormal body temperature and/or marked diurnal fluctuation, sweating episodes, recurrent feeling of feverishness and cold extremities; intolerance to heat and cold; marked weight change–anorexia or abnormal appetite; loss of adaptability and tolerance for stress, worsening of symptoms with stress and a slow recovery.

____ **Immune Manifestations:** tender lymph nodes, recurrent sore throat and flu-like symptoms, general malaise, new sensitivities to food, medications and/or chemicals.

☐ 7. **The illness persists for at least six months. It usually has a distinct onset,** **although it may be gradual.** Preliminary diagnosis may be possible earlier. Three months is appropriate for children.

1. "Crash" refers to a temporary period of immobilizing physical and/or mental fatigue.

To be included, the symptoms must have begun or have been significantly altered after the onset of the illness. It is unlikely that a patient will suffer from all symptoms in criteria 5 and 6. The disturbances tend to form symptom clusters that are often unique to a particular patient. The manifestations fluctuate and may change over time. Children often have numerous prominent symptoms but their order of severity tends to vary from day to day.

***There is a small number of patients who have no pain or no sleep dysfunction but no other diagnosis fits except ME/CFS. A diagnosis of ME/CFS should only be entertained when this group has an infectious illness type onset.**

****Some patients have been unhealthy for other reasons prior to the onset of ME/CFS and lack detectable triggers at onset and/or have more gradual or insidious onset.**

Exclusions: Confirm active disease processes that explain most of the major symptoms of fatigue, sleep disturbance, pain, and cognitive dysfunction. It is essential to exclude certain diseases, which would be tragic to miss: Addison's disease, Cushing's syndrome, hypothyroidism, hyperthyroidism, iron deficiency, iron overload syndrome, other treatable forms of anemia, diabetes mellitus, cancer. It is also essential to exclude treatable sleep disorders such as upper airway resistance syndrome and obstructive or central sleep apnea; rheumatological disorders such as rheumatoid arthritis, lupus, polymyosistis, and polymyalgia rheumatica; immune disorders such as AIDS; neurological disorders such as MS, Parkinsonism, myasthenia gravis and B12 deficiency; infectious diseases such as tuberculosis, chronic hepatitis, Lyme disease, etc; primary psychiatric disorders and substance abuse. Exclusion of other diagnoses, which cannot be reasonably excluded by the patient's history and physical examination, is achieved by laboratory testing and/or imaging. If a potentially confounding medical condition is under control, then the diagnosis of ME/CFS can be entertained if the patient meets the criteria otherwise.

Co-Morbid Entities: Fibromyalgia syndrome, myofascial pain syndrome, temporomandibular joint syndrome, irritable bowel syndrome, interstitial cystitis, irritable bladder syndrome, Raynaud's phenomenon, prolapsed mitral valve, migraine, allergies, multiple chemical sensitivities, thyroiditis, sicca syndrome, depression, Hashimoto's, etc. Such co-morbid entities may occur in the setting of ME/CFS. Others such as IBS may precede the development of ME/CFS by many years, but then become associated with it. The same holds true for migraines and depression. Their association is thus looser than between the symptoms within the syndrome. ME/CFS and FMS often closely connect and should be considered to be "overlap syndromes."

Idiopathic Chronic Fatigue: If the patient has unexplained prolonged fatigue but has insufficient symptoms to meet the criteria for ME/CFS, it should be classified as idiopathic chronic fatigue.

____________ **Patient meets the criteria for ME/CFS**
____________ **Patient meets the criteria for Idiopathic Chronic Fatigue**

NOTES: ____

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Reference: Carruthers, B. M., A. K. Jain, K. L. De Meirleir, D. L. Peterson, N. G. Klimas, A. M. Lerner, A. C. Bested, P. Flor-Henry, P. Joshi, A. C. P. Powles, J. A. Sherkey, M. I. van de Sande. "Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols." *Journal of Chronic Fatigue Syndrome*, 2003; 11(1):7–116.

THE AMERICAN COLLEGE OF RHEUMATOLOGY 1990 CRITERIA FOR THE CLASSIFICATION OF FIBROMYALGIA*

According to the revised 1990 Diagnostic Criteria for the Classification of Fibromyalgia, a patient is considered to have Fibromyalgia when all three of the following conditions are present.

1. History of widespread pain including all of the following:

positive ____/5

- ☐ left side of the body
- ☐ right side of the body
- ☐ above the waist
- ☐ below the waist
- ☐ axial

2. Report of pain by the patient in at least 11/18 tender point sites:

positive ____/18

[L]	[R]	occiput	[L]	[R]	supraspinatus	[L]	[R]	gluteal
[L]	[R]	low cervical	[L]	[R]	second rib	[L]	[R]	greater trochanter
[L]	[R]	trapezius	[L]	[R]	lateral epicondyle	[L]	[R]	knee

3. Duration of at least three months: duration________________

positive ____/1

Note:

- axial skeletal pain is considered to be cervical spine or anterior chest or thoracic spine or low back.
- shoulder and buttock pain is considered as pain for each side.
- low back pain is considered lower segment pain.
- digital palpation should be performed with an approximate force of 4 kilograms using the thumb or first and/or second finger.
- for a tender point to be considered positive subject must state that the palpation was painful.
- "tender" is not be considered "painful".
- the presence of a second clinical disorder does not exclude the diagnosis of Fibromyalgia.

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*The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia - Report of the Multicenter Criteria Committee, Wolfe, F., Smythe, H.A., Yunis, M.B., et.al., Arthritis and Rheumatism Volume 33, Number 2 (February 1990).

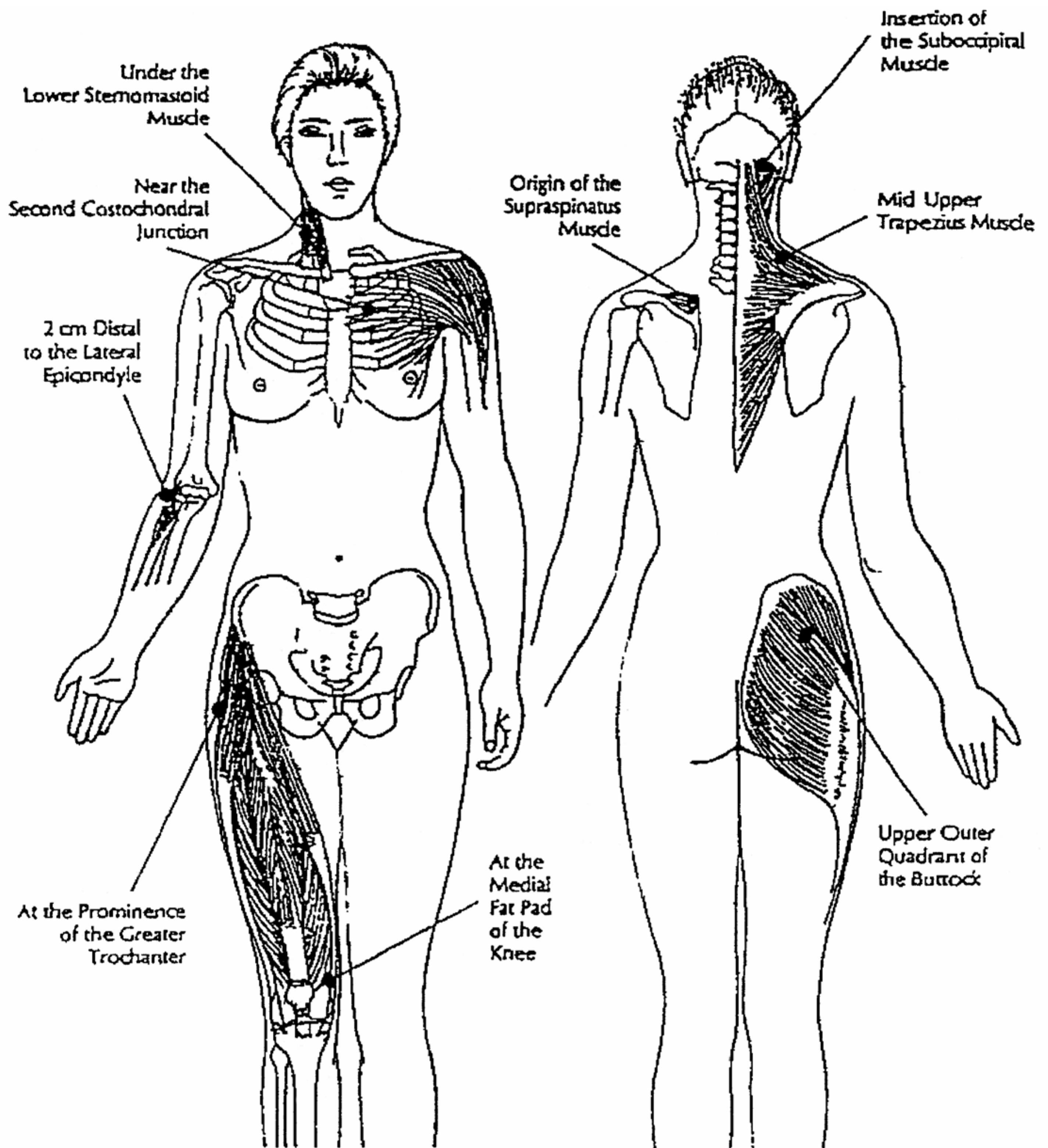

Fig. 5-1. Tenderness at characteristic musculoskeletal locations establishes fibromyalgia as a consistent entity. The nine "tender points" depicted are important in diagnosis: Each is bilateral, for a total of 18 test sites widely distributed on the body surface, and tenderness on digital palpation of at least 11 in a patient with at least a 3-month history of diffuse musculoskeletal pain is recommended as the diagnostic standard for fibromyalgia. [Reproduced with permission. From D. L. Goldenberg: Diagnostic and Therapeutic Challenges of Fibromyalgia. *Hosp. Practice* (office edition) 30 Sep 1989, 24:9A, P.45.]

Reference: Goldenberg, D. L. "Diagnostic and Therapeutic Challenges of Fibromyalgia." *Hosp Pract* (Off Ed), 1989 Sep 30;24(9A):39–52.

Multiple Chemical Sensitivity

Case Criteria Checklist

- ❒ The symptoms are reproducible with [repeated chemical] exposure.
- ❒ The condition is chronic.
- ❒ Low levels of exposure [lower than previously or commonly tolerated] result in manifestations of the symptom.
- ❒ The symptoms improve or resolve when the incitants are removed.
- ❒ Responses occur to multiple chemically unrelated substances.
- ❒ [Added in 1999]: Symptoms involve multiple organ systems.

Reference: 1999 Consensus on Multiple Chemical Sensitivity. Archives of Environmental Health, May/June 1999, Vol. 54, No. 3, based on: J. R. Nethercott, L. L. Davidoff, B. Curbow. “Multiple Chemical Sensitivities Syndrome: Toward a Working Case Definition.” *Arch Environ Health*, 1993; 48:19–26.

- ❒ Having a stronger sense of smell than others.
- ❒ Difficulty concentrating.
- ❒ Feeling dull or groggy.
- ❒ Feeling spacey.

Reference: McKeown-Eyssen, G. E., C. J. Baines, L. M. Marshall, et al. “Multiple Chemical Sensitivity: Discriminant Validity of Case Definitions.” *Arch Environ Health*, 2001; 56(5):406–12.