

 <p><b>INTERNATIONAL CONSENSUS CRITERIA (ICC) Diagnosis for Myalgic Encephalomyelitis (ME)</b></p>	<p><b>INSTITUTE OF MEDICINE (IOM) REPORT Beyond ME/CFS aka Systemic Exertion Intolerance Disease (SEID)</b></p> <p>IOM is now National Academy of Medicine</p>
<p><b>Immediate diagnosis</b></p>	<p><b>Six months wait period</b></p>
<p>ME is an acquired neurological disease with complex global dysfunctions. Pathological dysregulation of the nervous, immune and endocrine systems, with impaired cellular energy metabolism and ion transport are prominent features. Although signs and symptoms are dynamically interactive and causally connected, the criteria are grouped by regions of pathophysiology to provide general focus.</p> <p>Note: Per the ICC, ME is classified as a neurological disease by the World Health Organization under code G93.3.</p>	<p>A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities, that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest.</p>
<p><b>Post-Exertional Neuroimmune Exhaustion (PENE)</b></p> <p>This cardinal feature is a pathological inability to produce sufficient energy on demand with prominent symptoms primarily in the neuroimmune regions. Characteristics are:</p> <ol style="list-style-type: none"> <li>1. Marked, rapid physical and/or cognitive fatigability in response to exertion, which may be minimal such as activities of daily living or simple mental tasks, can be debilitating and cause a relapse.</li> <li>2. Post-exertional symptom exacerbation: e.g. acute flu-like symptoms, pain and worsening of other symptoms.</li> <li>3. Post-exertional exhaustion may occur immediately after activity or be delayed by hours or days.</li> <li>4. Recovery period is prolonged, usually taking 24 hours or longer. A relapse can last days, weeks or longer.</li> <li>5. Low threshold of physical and mental fatigability (lack of stamina) results in a substantial reduction in preillness activity level.</li> </ol> <p>For a diagnosis of ME, symptom severity must result in a significant reduction of a patient's premorbid activity level.</p>	<p><b>Post Exertion Malaise (PEM)*</b></p> <p>PEM is worsening of a patient's symptoms and function after exposure to physical or cognitive stressors that were normally tolerated before disease onset. Subjective reports of PEM and prolonged recovery are supported by objective evidence in the scientific literature, including failure to normally reproduce exercise test results (2-day cardiopulmonary exercise test) and impaired cognitive function after exertion. There is sufficient evidence that PEM is a primary feature that helps distinguish ME/CFS (SEID) from other conditions.</p> <p><small>* Frequency and severity of symptoms should be assessed. The diagnosis of ME/CFS (SEID) should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial, or severe intensity.</small></p>
<p><b>Sleep Disturbances:</b> Symptoms to choose from include:</p> <p>Disturbed sleep patterns: e.g. insomnia, prolonged sleep including naps, sleeping most of the day and being awake most of the night, frequent awakenings, awaking much earlier than before illness onset, vivid dreams/nightmares.</p> <p>Unrefreshed sleep: e.g. awoken feeling exhausted regardless of duration of sleep, day-time sleepiness.</p>	<p><b>Unrefreshing sleep *</b></p> <p>Despite the absence of a specific objective alteration in sleep architecture, the data are strong that the complaint of unrefreshing sleep is universal among patients... Diagnosis of a primary sleep disorder does not rule out a diagnosis of ME/CFS (SEID).</p>

## Neurological Impairments:

At least one symptom from 3 of the following 4 symptoms:

Neurocognitive impairment, pain, sleep disturbance, or neurosensory, perceptual and motor disturbances.

Impairments include:

**Difficulty processing information: slowed thought, impaired concentration.** E.g. confusion, disorientation, cognitive overload, difficulty with making decisions, slowed speech, acquired or exertional dyslexia.

**Short-term memory loss:** e.g. difficulty remembering what one wanted to say, what one was saying, retrieving words, recalling information, poor working memory.

**IC primer:** "Spinal cord and ganglia - (autopsy): Increased neuroinflammation in the dorsal root ganglia, (modulators of peripheral sensory information traveling to the brain)."

"Profound dysfunction/dysregulation of the neurological control system results in faulty communication and interaction between the CNS and major body systems, notably the immune and endocrine systems, dysfunction of cellular energy metabolism and ion transport, and cardiac impairments."

## Cognitive impairment \*

Cognitive impairment or Orthostatic Intolerance for diagnosis

Cognitive impairment in ME/CFS (SEID) includes problems with thinking or executive function exacerbated by exertion, effort, or stress or time pressure. There is sufficient evidence that slowed information processing is common in patients with ME/CFS (SEID), and a growing body of evidence shows that it may play a central role in overall neurocognitive impairment associated with the disease (memory impairments, attention deficits, and impaired psychomotor function). Such a deficit may be responsible for disability that results in loss of employment and loss of functional capacity in social environments.

## Energy Metabolism/Ion Transportation Impairments:

At least one symptom

1. Cardiovascular: e.g. inability to tolerate an upright position - orthostatic intolerance (OI), neurally mediated hypotension (NMH), postural orthostatic tachycardia syndrome (POTS), palpitations with or without cardiac arrhythmias, light-headedness/dizziness.
2. Respiratory: e.g. air hunger, laboured breathing, fatigue of chest wall muscles.
3. Loss of thermostatic stability: e.g. subnormal body temperature, marked diurnal fluctuations; sweating episodes, recurrent feelings of feverishness with or without low grade fever, cold extremities.
4. Intolerance of extremes of temperature.

## Orthostatic Intolerance (OI)

Cognitive impairment or Orthostatic Intolerance for diagnosis

Symptoms are improved, although not necessarily abolished, by lying back down or elevating the feet. Sufficient evidence indicates a high prevalence of orthostatic intolerance conditions in ME/CFS (SEID) as measured by objective heart rate and blood pressure abnormalities and physical findings during standing, bedside orthostatic vital signs, head-up tilt testing, or by patient-reported exacerbation of orthostatic symptoms with standing in day-to-day life. These findings indicate that OI is a common and clinically important finding in ME/CFS (SEID).

**The IOM does not recognize any further symptoms for diagnostic purposes.**

## ICC CONTINUED

ICC is far more extensive providing for more detailed symptoms and consistent guidelines for diagnosing ME patients.

**While the following symptoms are not recognized by the IOM for diagnostic purposes, they are occasionally mentioned throughout the clinician's guide.**

<p><b>PAIN:</b></p> <p>Headaches: e.g. chronic, generalized headaches often involve aching of the eyes, behind the eyes or back of the head that may be associated with cervical muscle tension; migraine; tension headaches.</p> <p><b>Significant pain can be experienced in muscles,</b> muscle-tendon junctions, joints, abdomen or chest. It is noninflammatory in nature and often migrates. e.g. generalized hyperalgesia, widespread pain (may meet fibromyalgia criteria), myofascial or radiating pain.</p> <p>Pain is included in PENE.</p>	<p><b>PAIN:</b></p> <p>Pain is common but highly variable in presence, nature, and severity (with a higher prevalence in more severe cases).</p> <p>However, there is no conclusive evidence that pain experienced by patients can be distinguished from that experienced by healthy people or those with other diseases. Pain can come in many forms, including headaches, arthralgia, and myalgia.</p> <p>Fibromyalgia listed under comorbid conditions</p>
<p><b>Neurosensory, Perceptual and Motor Disturbances:</b></p> <p>E.g. inability to focus vision, sensitivity to light, noise, vibration, odour, taste and touch; impaired depth perception.</p> <p>Motor: e.g. <b>muscle weakness</b>, twitching, poor coordination, feeling unsteady on feet, ataxia.</p>	<p><b>Neither neurosensory, perceptual nor motor disturbances included in IOM guide for clinicians.</b></p> <p>General description of disease severity: <i>“Severely affected patients may need to lie down while they are being interviewed.”</i></p>
<p><b>Immune, Gastro-intestinal &amp; Genitourinary Impairments</b></p> <p>At least one symptom from three of the following five symptom categories.</p> <ol style="list-style-type: none"> <li>1. Flu-like symptoms may be recurrent or chronic and typically activate or worsen with exertion. e.g. sore throat, sinusitis, cervical and/or axillary lymph nodes may enlarge or be tender on palpitation.</li> <li>2. Susceptibility to viral infections with prolonged recovery periods.</li> <li>3. Gastro-intestinal tract: e.g. nausea, abdominal pain, bloating, irritable bowel syndrome (IBS).</li> <li>4. Genitourinary: e.g. urinary urgency or frequency, nocturia.</li> <li>5. Sensitivities to food, medications, odors or chemicals.</li> </ol>	<p><b>Immune System not diagnostic in IOM</b></p> <p>...the committee’s literature search yielded data demonstrating poor NK cell cytotoxicity that correlates with illness severity...although it is not specific to ME/CFS (SEID). There is also insufficient evidence for an association between ME/CFS and bacterial, fungal, parasitic, and other viral infections.... other symptoms that may support a diagnosis of ME/CFS (SEID). These include Gastrointestinal impairments • Genitourinary impairments • Sore throat • Painful or tender axillary/cervical lymph nodes • Sensitivity to external stimuli (e.g., foods, drugs, chemicals). IBS listed under possible comorbid conditions.</p>
<p><b>Energy Metabolism/Ion Transportation Impairments:</b> At least one of the following symptoms:</p> <p>Cardiovascular, Respiratory, Loss of thermostatic stability, or Intolerance of extremes of temperature.</p>	<p><b>Neither cardiac issues, respiratory issues, nor thermostatic instability included in IOM guide for clinicians.</b></p>
<p><b>Testing and Exclusions:</b></p> <p>ICC lists many lab tests to aid in diagnosis. Alternate explanatory diagnosis is achieved by the patient’s history, physical examination, and laboratory/biomarker testing as indicated. Primary psychiatric disorders, somatoform disorder and substance abuse are excluded.</p>	<p><b>NO LAB TESTS LISTED</b></p> <p><b>NO EXCLUSIONS LISTED</b></p>