

**SUPPLEMENTAL TABLE 1.****Potentially Abnormal Physical Examination Findings in ME/CFS<sup>a</sup>**

<b>Physical Exam Category</b>	<b>Possible Abnormal Findings</b>
Overall appearance	<ul style="list-style-type: none"><li>• Fatigability over the course of a visit</li><li>• Inability to maintain cognitive focus</li><li>• Worsening of symptoms</li><li>• Need to lay down during visit</li><li>• Use of eyeglasses/ear plugs to minimize light/sound sensitivity</li><li>• Pallor</li></ul>
Vital signs	<ul style="list-style-type: none"><li>• Low-grade fever</li><li>• Elevated heart rate and/or blood pressure drop with orthostatic testing or 10-minute passive standing test<sup>1</sup></li><li>• Increased respiratory rate</li></ul>
Head, eyes, ear, nose, throat	<ul style="list-style-type: none"><li>• Pupillary oscillation when eyes exposed to light</li><li>• Enlarged and/or tender cervical lymph nodes</li><li>• Crimson crescents or striae in pharynx which may worsen after a passive standing test</li></ul>
Abdominal	<ul style="list-style-type: none"><li>• Abdominal tenderness</li></ul>

Musculoskeletal	<ul style="list-style-type: none"> <li>• Multiple tender joints without redness, warmth, or swelling</li> <li>• Tender muscles</li> </ul>
Extremities	<ul style="list-style-type: none"> <li>• Cold hands and feet</li> <li>• Axillary lymphadenopathy</li> </ul>
Neurologic	<ul style="list-style-type: none"> <li>• Allodynia/hyperalgesia</li> <li>• Reduced pinprick/ thermal/ vibratory sensation</li> <li>• Confusion</li> <li>• Difficulty asking/answering questions, concentrating and performing multiple, simultaneous tasks</li> <li>• Abnormal Romberg</li> </ul>
<p><sup>a</sup> Most patients will have an unremarkable physical examination; an abnormal finding is not required for diagnosis.</p>	

**SUPPLEMENTAL TABLE 2:****Tests to Be Considered Depending on Presentation<sup>a</sup>**

These are general recommendations to identify alternative diagnoses and comorbidities dependent on the patient's particular presentation and may be ordered by primary care providers or specialists as appropriate. For more information on these and other tests and when they would be ordered, see the referenced document.

<b>Type of Disorder</b>	<b>Tests</b>
Autonomic Disorders	Passive standing test, tilt table test, capnography <sup>b</sup>
Rheumatological Disorders	Antinuclear antibody, rheumatoid factor, creatine kinase Early Sjogren's panel, SSA, SSB in patients with dry eyes, mouth <sup>b</sup>
Infectious Disease	Epstein-Barr virus antibody panel, cytomegalovirus antibody panel, human immunodeficiency virus test, hepatitis B antibody panel, hepatitis C antibody panel, purified protein derivative skin test or interferon gamma release assays, rapid plasma reagin or treponemal antibody test, West Nile serum IgM and IgG antibody, parvovirus B19 vector-borne disease, <sup>b</sup> anti-streptolysin O titer <sup>b</sup>

Oncological Disorders	Specific screening and tests based on symptoms, physical signs, and/or risk factors
Cardiovascular/ Pulmonary Disorders	Chest x-ray, pulmonary function tests, electrocardiogram, trans-thoracic echocardiography, arrhythmia monitoring, exercise testing for coronary artery disease
Neurological Disorders	Magnetic resonance imaging of brain (T2 weighted), cervical spine, or lumbar spine; lumbar puncture; and other imaging as appropriate if evidence of neurological symptoms/signs <sup>b</sup>
Allergies	Histamine, tryptase and chromogranin A, allergy skin tests or radioallergosorbent test in patients with allergies <sup>b</sup>
Immunological Disorders	Total immunoglobulins, IgG subclasses in patients with prolonged or frequent infections <sup>b</sup>
Endocrine/ Metabolic Disorders	Hemoglobin A1c if evidence of elevated glucose, suspicion of diabetes <sup>b</sup> Parathyroid hormone, ionized calcium in older patients. <sup>b</sup> Follicle stimulating hormone if patient may be peri or post-menopause. <sup>b</sup> Free and total testosterone if evidence of hypogonadism. <sup>b</sup> Adrenocorticotrophic hormone if abnormal AM cortisol and evidence of adrenal insufficiency or Cushing's syndrome <sup>b</sup>

Gastrointestinal Disorders	Esophagogastroduodenoscopy, colonoscopy, food sensitivity tests as appropriate <sup>b</sup>
Pain	Small punch biopsy of skin in patients with evidence of neuropathy, widespread hyperalgesia <sup>b</sup>
Psychiatric Disorders	Clinical psychiatric screens; recommend those with less emphasis on somatic symptoms to avoid misdiagnosis as a mental illness (e.g. Patient Health Questionnaire-4, Generalized Anxiety Disorder Scale-7)
Sleep	Home sleep studies, polysomnography
Miscellaneous	Vitamin B6 if clinical concern for neuropathy or patient taking vitamin B6 supplements <sup>b</sup>
<p><sup>a</sup> Adapted from Testing Recommendations for Suspected ME/CFS authored by the US ME/CFS Clinician Coalition.<sup>2</sup> Reproduced with their permission.</p> <p><sup>b</sup> Followup tests that are typically used later in the diagnostic process</p>	

**SUPPLEMENTAL TABLE 3.****Conditions Which Commonly Co-exist with ME/CFS<sup>a</sup>**

Autonomic Dysfunction	Rheumatological Disorders	Neurological Disorders
Postural orthostatic tachycardia syndrome, neurally mediated hypotension, orthostatic hypotension	Fibromyalgia, <sup>b</sup> Ehlers-Danlos syndrome, temporomandibular joint dysfunction, sicca syndrome	Sensory hypersensitivities, <sup>c</sup> poor balance, migraine headaches, peripheral neuropathy, small fiber neuropathy
Immunological Disorders	Gastrointestinal Disorders	Endocrine/Metabolic Disorders
New or worsened allergies, mast cell activation syndrome, multiple chemical sensitivities, chronic infections & immunodeficiencies	Food allergies/intolerances, <sup>d</sup> gut motility issues, celiac disease, irritable bowel syndrome, small intestinal bacterial overgrowth	Hypothyroidism, hypothalamus-pituitary-adrenal axis dysregulation, <sup>e</sup> metabolic syndrome
Sleep Disorders	Psychiatric Disorders	Gynecological Disorders

Sleep apnea, restless leg syndrome, periodic limb movement disorder	Secondary anxiety, secondary depression	Endometriosis, premenstrual syndrome, vulvodynia
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Miscellaneous

Interstitial cystitis, overactive bladder, nutritional deficiencies (e.g. vitamin B12, D), obesity

<sup>a</sup> Adapted from Diagnosing and Treating Myalgic Encephalomyelitis/Chronic Fatigue syndrome (ME/CFS) authored by the US ME/CFS Clinician Coalition.<sup>3</sup> Reproduced with their permission.

<sup>b</sup> People with fibromyalgia without ME/CFS do not experience post-exertional malaise and the worsening after exercise seen in ME/CFS. As a result, they can be helped by exercise. Fibromyalgia is associated with widespread muscle pain, which may not be seen in ME/CFS patients who do not have fibromyalgia. See Table 1 and the Institute of Medicine Report Guide for Clinicians for questions to assess post-exertional malaise.<sup>4</sup> An 18-point tender point exam can be used to evaluate the widespread pain seen in fibromyalgia.

<sup>c</sup> To light, sound, touch, smell, etc.

<sup>d</sup> Intolerance to certain foods, including gluten, sugar, and milk protein is not rare.

<sup>e</sup> Low-normal or flattened cortisol curve upon awakening.

## References

1. Bateman L. "Simple way to assess orthostatic intolerance." Bateman Horne Center. Published September 2016. <http://batemanhornecenter.org/assess-orthostatic-intolerance/> Accessed December 26, 2020.
2. US ME/CFS Clinician Coalition. Testing recommendations for suspected ME/CFS. Published February 20, 2021. <https://mecfscliniciancoalition.org/mecfs-clinician-coalition-testing-recs-v1> Accessed March 3, 2021.
3. US ME/CFS Clinician Coalition. Diagnosing and treating myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Published July 2020. <https://mecfscliniciancoalition.org/mecfs-clinician-coalition-dx-tx-handout-v2> Accessed January 20, 2021. Also available in multiple languages on the US ME/CFS Clinician Coalition website - <https://mecfscliniciancoalition.org/> Accessed on January 20, 2021
4. US Institute of Medicine. Beyond myalgic encephalomyelitis/chronic fatigue syndrome: redefining an illness. Report guide for clinicians. The National Academies Press. February 2015. <https://www.nap.edu/resource/19012/MECFSciniciansguide.pdf> Accessed December 26, 2020.