

Medical considerations when treating urgently ill patients with underlying myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

The intention of this handout is to provide basic advice and medical/scientific information about ME/CFS that can inform medical decisions in urgent, emergent, or hospital settings. Each page builds upon the next and has been separated for ease of review.

ME/CFS is a chronic, multisystem illness whose presence may impact decisions regarding diagnostic studies and medical interventions.

ME/CFS is characterized by severe fatigue and easy fatigability for both physical and cognitive tasks propagated by low energy reserves and pathologically altered metabolism.

Symptoms can worsen after physical, cognitive and emotional effort, as well as orthostatic, environmental, and sensory stress. **When subjected to these stressors, patients may experience a flare of exhaustion, cognitive impairment, pain and sensory amplification, headaches, autonomic dysregulation, dizziness, flu-like symptoms, or even non-epileptic seizures related to diffuse cerebral hypoperfusion.**

Common comorbid conditions in ME/CFS that may be responsible for flares or driving presenting symptoms include:

- Mast cell activation syndrome
- Small fiber polyneuropathies
- Postural orthostatic tachycardia syndrome (POTS)
- Gastrointestinal dysautonomia and functional GI dysmotility
- Pain amplification disorders (to include fibromyalgia)
- Multiple chemical or sensory sensitivities
- Primary sleep disorders
- Small intestine bacterial overgrowth (SIBO)
- Cranio-cervical instability
- Hypermobility Ehlers's Danlos syndrome
- Sicca syndrome
- Celiac disease
- Autoimmune thyroid disease, euthyroid sick syndrome

QUICK TIPS for managing patients with ME/CFS who become acutely ill

Presume the patient is orthostatic and treat as if in “hypovolemic shock” (abnormal perfusion and circulatory failure)

- Increase and maintain intravascular volume with IV saline (even when peripheral edema is present, as this is often 2/2 venous preload failure with secondary peripheral third spacing). Monitor orthostatic vital signs. Monitor and replace electrolytes. Consider alternating NS and LR. Avoid hypotension and hypovolemia. Albumin is not required in most instances.
- Provide oxygen even if not severely hypoxemic. SpO2 levels could be falsely depressed as a function of poor peripheral circulation (such as is seen with Raynaud’s).
- Allow patients to lie down, or sit with feet elevated, limit activity and rest as needed. Avoid prolonged standing, or even sitting with feet on the floor. Provide a wheelchair for energy conservation when mobilizing.

Reduce sensory stimuli (sensory stress) as much as possible

- Reduce: bright light, loud music, obnoxious sounds, scents/odors.
- Maintain adequate pain control.
- Limit nighttime sleep disruptions, such as laboratory testing. Treat sleep, if needed and appropriate. Serial nights of sleep disruption may worsen ALL aspects of illness.

Assume waxing and waning cognitive impairment (cognitive slowing) is present

- Keep conversation simple. Avoid compound questions.
- Be patient and allow longer periods for patient responses to questions. Word-finding difficulties are common.
- Write down instructions.
- Allow family and caregivers to aid with communication.

Use medications thoughtfully and skillfully with close monitoring

- Patients with ME/CFS may be unusually sensitive to medication effects and more likely to have intolerances or allergic reactions. Medication side effects may be related to an exaggerated sympathetic nervous system response to foreign substances and not reflect known pharmacological side effects of medications.
- Start low (10 - 25% of usual) with medication doses. Consider past intolerances and experiences.
- Be cautious about abruptly stopping benzodiazepines and opioids, as the withdrawal can be amplified and dramatically provoke rebound symptoms.
- Consider "stress doses" of hydrocortisone (5-10 mg bid) as though the patient has adrenal insufficiency. Though cortisol levels may be normal, cellular response to normal cortisol levels is often downregulated.

The current evidence-based core clinical diagnostic criteria for ME/CFS (symptoms must be moderate to severe and present 50% of the time for at least 6 months) are: impaired ability to function in association with fatigue, post-exertional illness worsening, disordered sleep, cognitive impairment and/or orthostatic intolerance. Most patients also experience pain and immune manifestations. <https://pubmed.ncbi.nlm.nih.gov/25695122/>

Based on current evidence the underlying pathology of ME/CFS involves energy metabolism, the nervous system, and the immune system(1).

Abnormal cellular metabolism. Metabolomics have found deficits in pathways that generate energy from simple sugars, fatty acids, and amino acids. Increased lactate levels in cerebrospinal fluid may indicate impaired oxidative phosphorylation, with a consequent shift to anaerobic metabolism. Cardiopulmonary exercise testing (CPET) testing suggests a low anaerobic threshold. Invasively monitored CPET demonstrates impaired/reduced pre-load and reduced oxygen extraction from either perfusion abnormalities or inability of cells to utilize delivered oxygen.

Neuroinflammation and central sensitization. Amplification of, or increased sensitivity to, sensory stimuli. Spinal fluid studies have shown elevated WBC and protein. MRI, functional MRI, and PET studies have revealed hypoperfusion, elevated lactate, and widespread activation of glial cells and astrocytes. EEG studies show abnormal brain waves and connectivity of various brain regions.

Cognitive impairment. High quality evidence supports cognitive slowing, deficits in attention, memory, and reaction time. It is unclear how much this relates to a neuroinflammatory process versus impaired brain perfusion.

Impaired/dysregulated HPA-axis and ANS stress response. Orthostatic intolerance is common. Neuroendocrine studies demonstrate abnormalities of the hypothalamic-pituitary-adrenal axis, of growth hormone secretion, and central signaling of cortisol release. ANS studies have found strong evidence of disordered autonomic nervous system activity, impaired baroreflex function, exaggerated venous pooling, diminished red cell mass, and reduced plasma volume.

Abnormal immune function. Evidence supports impaired natural killer cell function, increased numbers of activated CD8+ cytotoxic T cells, presence of various autoantibodies, particularly to targets in the CNS and ANS. Increased production of various proinflammatory cytokines correlate with illness severity. Mast cell activation is present in many patients.

Risk of viral reactivation (for example: varicella zoster, CMV, EBV, COVID-19, enteroviruses) may be present.

This handout was prepared in Jan. 2022 by Lucinda Bateman, MD, and Brayden Yellman, MD, of the Bateman Horne Center. It is intended to raise awareness about known aspects of ME/CFS. The tips are from Dr. Bateman and Yellman, experts in the management of ME/CFS. There are currently no treatment guidelines for ME/CFS, although expert consensus guidance has been published (2). Every case should be carefully assessed and treated using the best judgement of the managing physician, and for each presenting medical problem, taking current scientific progress and guidance into account.

RESOURCES:

Inflammation correlates with symptoms in chronic fatigue syndrome. Komaroff AL. Proc Natl Acad Sci USA. 2017 Aug 22; 114(34): 8914-8916. Published online 2017 Aug 15. doi: 10.1073/pnas.1712475114 PMCID: PMC5576849

ME/CFS: Essentials of Diagnosis and Management. Bateman L, et al. Mayo Clinic Proc. 2021 Nov 01. Vol 96, Issue 11, P2861-78. DOI: <https://doi.org/10.1016/j.mayocp.2021.07.004>. Open Access