

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: What Every Family Physician Needs to Know - By Mary Dimmock, Susan Levine, MD, and Terri L. Wilder, MSW

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Introduction

Myalgic encephalomyelitis (ME), also known as chronic fatigue syndrome (CFS) or ME/CFS remains an elusive diagnosis to most family and primary care practitioners. There are currently no Federal Drug Administration (FDA) approved treatments specific to this disease. Clinical guidance has often recommended cognitive behavioral (CBT) and graded exercise therapy (GET), but these therapies are inappropriate and potentially harmful for patients with ME/CFS.

In 2015, the Institute of Medicine (IOM, now called the National Academy of Medicine) issued new clinical diagnostic criteria for ME/CFS and summarized the growing evidence of biological impairment. Since then, the National Institutes of Health (NIH) has funded three Centers of Excellence to study ME/CFS, a pediatric ME/CFS primer has been published, and the Centers for Disease Control (CDC) has updated the diagnostic and treatment information on its website.

Family physicians have a critical role to play in providing early diagnosis and effective treatment of this disabling disease.

History

ME/CFS has existed throughout the twentieth century but has been both maligned and misunderstood as a result of a lack of research, a paucity of diagnostic tests and FDA approved treatments, and because of non-specific diagnostic criteria that included patients with other diseases. As a result, patients with ME/CFS have remained unidentified or have been misdiagnosed and thus have struggled to get proper clinical care.

Further complicating our understanding of ME/CFS, a significant number of ME/CFS research studies have focused on the role of psychogenic factors in the development and perpetuation of the disease. These studies were based on the unproven theory that the severity and poor prognosis of ME/CFS was due to the patients' harboring a fear of activity and thus becoming deconditioned and that these could be reversed with CBT and GET. Unfortunately, the most commonly recommended treatments in ME/CFS clinical guidance have been CBT and GET, based on these false presumptions.

Other researchers have focused on evidence of biological pathology across multiple systems, including the characteristic abnormal response to exertion. In 2015, IOM reviewed the published evidence for the biological underpinning of ME/CFS and concluded that the disease is not psychological or due to deconditioning.

Based on the findings of more than ten thousand peer-reviewed articles published worldwide, it is clear that ME/CFS is a chronic, multi-system disease associated with neurological, neurocognitive, immunological, autonomic, and aerobic energy metabolism impairment. The IOM report called attention to the disease's hallmark symptoms, such as post-exertional malaise (PEM), a delayed exacerbation of symptoms and a loss of stamina following even trivial cognitive or physical exertion.

To address the problem of under- and misdiagnosis, the IOM report also established new clinical diagnostic criteria, which require the presence of the following core symptoms: substantial impairment in activity accompanied by exhaustion; post exertional malaise;

unrefreshing sleep and neurocognitive or autonomic dysfunction, all of which must have been present for at least 6 months.

Supporting the conclusions of the IOM report, the Agency for Healthcare Research and Quality (AHRQ, part of Health and Human Services) published a 2016 addendum to a 2014 evidence review that downgraded the 2014 recommendations for CBT and GET, because the supporting studies had included patients with other 'fatiguing' illnesses. AHRQ also reported that harms were generally underreported but that GET trials were "associated with higher numbers of reported adverse events." Patient surveys have also reported a worsening of symptoms following both GET and CBT.

Since the IOM report, the NIH has undertaken an intensive intramural study to better characterize the pathophysiology of the disease and in September 2017 awarded a 5-year, \$35 Million grant to three centers to spur research and effective collaboration among researchers, clinicians and the ME/CFS patient community. Two of these centers are in New York, at Columbia's Mailman School of Public Health and at Cornell University. Also in 2017, a pediatric ME/CFS primer was published providing specific guidelines for the diagnosis and treatment of this disease in children and adolescents and the CDC updated its ME/CFS website, adopting the IOM's clinical diagnostic criteria and removing CDC's earlier recommendations for CBT and GET.

Demographics and Presentation

ME/CFS is believed to affect approximately one million Americans, but quality epidemiological studies are limited and the actual disease prevalence could be higher. The IOM reported an estimated prevalence of 1 to 2.5 Million Americans, which amounts to 62,000 to 125,000 in New York State. ME/CFS affects more women than men and affects people of all socioeconomic backgrounds, age ranges and ethnic and racial diversity. There are no simple diagnostic tests or biomarkers, and there are no FDA approved treatments specific to this disease. The IOM report estimated that as many as 84-91% of patients are not diagnosed.

The onset of ME/CFS is often sudden, typically following a viral or other type of infection but may occur following other types of physical trauma. In other cases the disease may develop gradually, over a period of weeks or months. Patients describe feeling 'flu-like' symptoms chronically.

In addition to the characteristic postexertional malaise (PEM), patients may also experience cognitive impairment, unrefreshing sleep, autonomic manifestations, such as heart rate variability and excessive sweating, and also experience muscle and joint pain and sound, light, and chemical sensitivity. Elevated antibody titers to viruses may be present, in addition to low levels of autoimmune serology.

ME/CFS can present with a wide range of severity. Even in the same patient, the level of severity can change over time and from day to day as symptoms wax and wane. People with ME/CFS are unable to go about their daily activities in a predictable or consistent manner. The IOM report stated that up to 70% of patients are unable to work and one quarter remain bed- or housebound (the latter however may be an underestimate).

The IOM report stated that patients with ME/CFS are more functionally impaired than those with "type 2 diabetes mellitus, congestive heart failure, hypertension, depression, multiple sclerosis, and end-stage renal disease."¹⁵ Caring for severely disabled patients can put an enormous fiscal and emotional strain on family members and other caretakers. Recovery is rare and as a result, patients can remain ill for decades. The IOM report estimated burden on the American economy is \$17-24 billion annually in lost productivity and in direct medical costs.

Clinical Diagnosis

Previously, ME/CFS was considered a diagnosis of exclusion but the IOM criteria provide for the presence of certain “core” criteria in order to make the diagnosis of this disease. The IOM clinical diagnostic criteria for ME/CFS require:

- A substantial impairment in ability to engage in activity that lasts six months or more, is accompanied by fatigue, is not lifelong, is not the result of ongoing exertion and is not alleviated by rest
- Post-exertional malaise
- Unrefreshing sleep
- At least one of cognitive impairment or orthostatic intolerance

Sleep studies may identify co-morbid sleep apnea whereas the results of a tilt table test can confirm the presence of Postural Orthostatic Tachycardia Syndrome (POTS). Neuropsychiatric testing typically shows impaired working memory and slowed information processing. Querying the patient’s response the day after activities that were previously tolerated can help determine the presence of post-exertional malaise (PEM). The 2-day cardiopulmonary test (CPET) is used to measure anaerobic threshold, which is reduced in this disease and confirms the seminal finding of PEM.

A number of co-morbidities can be seen in ME/CFS, the most common of which include fibromyalgia, POTS, mast cell disturbances, and certain autoimmune disorders. These will need to be managed as appropriate for each condition.

Treatment

As noted above, there are no FDA approved treatments for ME/CFS. However, there are interventions that the family physician can provide to help patients with this disease. First and foremost, the family physician can explain post-exertional malaise and the associated aerobic metabolism impairment. For some people, exertion as minor as tooth brushing or eating can trigger PEM and a crash.

People with ME/CFS should not exceed their “energy envelope” and they should use an activity management approach called “pacing” to not exceed their limits. Family physicians can also prescribe therapies that relieve symptoms, including those for sleep, pain, and orthostatic intolerance, including IV saline and Florinef. For patients with elevated viral titers, antiviral medications can help reduce symptoms. Patients often use earphones, earplugs, sunglasses, and eye masks to relieve the sensitivities to light and sound.

Family physicians can also support patients by explaining the disease to the family and supporting applications for disability. Social security accepts the 2-day CPET as objective evidence to support a disability claim. If this test is not easily available, a thorough explanation from the clinician caring for a patient with ME/CFS that describes the patients’ daily activities may suffice.

Conclusions

Family physicians have an important role to play in the diagnosis and care of people with ME/CFS. In May 2017, New York State Commissioner of Health Dr. Howard Zucker sent a letter to NYS physicians encouraging them to include ME/CFS as part of the differential diagnosis when evaluating patients with these symptoms.

The clinical diagnostic criteria published by the Institute of Medicine (IOM) are an important tool in this differential diagnosis that can result in faster and more accurate diagnosis. They can also

provide the basis for treatment recommendations that can relieve symptoms and minimize postexertional crashes.

Most importantly, the family physician can validate the patient's experience and ensure that the patient is not harmed by inappropriate treatment recommendations for exercise or talk therapy intended to convince the patient they are not ill.