

# A Case Definition for Children with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

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**Abstract:** The case definition for chronic fatigue syndrome was developed for adults (Fukuda et al. 1994), and this case definition may not be appropriate for use with children and adolescents. The lack of application of a consistent pediatric definition for this illness and the lack of a reliable instrument to assess it might lead to studies which lack sensitivity and specificity. In this article, a case definition is presented that has been endorsed by the International Association of ME/CFS.

**Keywords:** myalgic encephalomyelitis, chronic fatigue syndrome, case definition

## A Case Definition for Children with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

Among adolescents, easy fatigability and disturbed learning and memorization are several characteristics of chronic fatigue syndrome (Miike et al. 2003). The fatigue may be quite severe and another feature of this illness is the individuality of symptom patterns and unpredictability of symptom severity. In a community-based study that occurred in Wichita, Kansas, Jones et al. (2004) estimated CFS-like pediatric prevalence rates to be 338 per 100,000, whereas in another community based study in Chicago, Jordan et al. (2006) found 60 cases per 100,000. In general, the prognosis for a child or adolescent diagnosed with CFS has been considered to be better than with adults with this diagnosis (Smith and Carter, 2003).

Currently, the Fukuda et al. criteria (1994) have been used to diagnose chronic fatigue syndrome in both adults and children. A clinical case definition has also been developed for ME/CFS (Myalgic Encephalomyelitis/chronic fatigue syndrome) (Carruthers et al. 2003), and one study found that the Canadian clinical ME/CFS case definition identified patients with more fatigue, weakness, neurological and neuropsychiatric symptoms than does the Fukuda et al. (1994) criteria (Jason et al. 2004). Unfortunately, both the Fukuda et al. (1994) and Canadian clinical ME/CFS case definition were developed for an adult population rather than a pediatric sample. And yet, most studies of young people with ME/CFS have used the Fukuda et al. adult criteria. However, children with the illness may exhibit a different symptomology than adults with ME/CFS (Jordan et al. 1997). Symptoms such as abdominal pain may be frequently present in pediatric ME/CFS, but may not be as common in adults. Bell (1995) reported that the three most common complaints, besides fatigue, in children and adolescents with ME/CFS were headaches, sleep disturbance, and cognitive difficulties. There clearly is a need to develop a pediatric definition of ME/CFS which allows for the application of consistent and objective criteria. Such a case definition may serve to stimulate research which will then not only further test the validity of this case definition but also elucidate pathophysiology and improve treatment approaches.

The International Association of Chronic Fatigue Syndrome has recently endorsed a ME/CFS Pediatric Case Definition (Jason et al. 2006) for those under the age of 18. A new assessment tool was also created by the International Association of Chronic Fatigue Syndrome working group, the DePaul Pediatric Health Questionnaire (DPHQ). The DPHQ is a self-report measure used to assess ME/CFS among

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children who are under the age of 18 years old (see <http://www.iacfsme.org/Portals/0/pdf/DePaulPediatricHealthQuestionnaire.pdf>).

### ME/CFS pediatric case definition

It is critical that those conducting studies attempting to diagnose children with ME/CFS carry out a thorough evaluation, including a comprehensive medical and developmental history, physical examination, and laboratory tests to confirm diagnosis. The history should involve both the parents as well as the child because children are still constructing their identity.

The definition presented has elements of the Fukuda et al. (1994) adult case definition, along with the recommendations of Reeves et al. (2003). We have also incorporated the structure of a new clinical case definition for ME/CFS that has been developed in Canada (Carruthers et al. 2003). We believe that requiring certain symptoms does provide more specification of critical symptoms for a case definition. However, we have tried to limit the types of symptoms within each of the Canadian criteria categories to allow investigators to more reliably categorize pediatric patients. We also believe that this case definition does reduce the prominence of the symptom fatigue and more explicitly highlights the importance of symptoms such as dizziness, pain, and flu-like symptoms.

Below we present a pediatric case definition for ME/CFS. To be diagnosed with pediatric ME/CFS, the child or adolescent must have clinically evaluated, unexplained, persistent or relapsing chronic fatigue over the past 3 months that is not the result of ongoing exertion; is not substantially alleviated by rest; results in substantial reduction in previous levels of educational, social and personal activities; and must persist or reoccur for at least three months. The three month criteria is in contrast to the six month criteria that exists with the adult Fukuda et al. case definition. The Canadian criteria suggest that children with symptoms lasting more than three months duration can be diagnosed with the illness (Carruthers et al. 2004). We agree with this notion, as Fowler, Duthie, Thapar, and Farmer (2005) did not find differences between 8–17 years olds with 3 versus 6 months of chronic fatigue.

The adult Fukuda et al. (1994) criteria definition required that the fatigue not be lifelong and that it be of a new and definite onset. We did not use this criterion because children and their

families may not be able to pinpoint a definite onset. The Fukuda et al. (1994) case definition also had the provision that the symptoms such as sore throat or memory impairment not predate the fatigue, but we also did not use this criterion as it has been found that, in children with an insidious onset, such symptoms may in fact predate fatigue.

### Critical symptoms

In addition, the children must have the concurrent occurrence of the following classic ME/CFS symptoms, which must have persisted or recurred during the past three months of illness (symptoms may predate the reported onset of fatigue). Support for the inclusion of these symptoms emerged from Rowe and Rowe's (2002) confirmatory factor analysis, which found muscle pain and fatigue, neurocognitive, abdominal, head and chest pain, neurophysiological, and immunological factors. We recommend using the Pediatric ME/CFS Questionnaire, which provides a way of gathering this information to help diagnose pediatric ME/CFS (Jason et al. 2006). It is generally recommended that adolescents age 12 and older fill it out themselves, and parents can assist or fill it out for children 11 and under. Some children might need to complete the questionnaire over several days if this task being completed at one testing might exacerbate the children's symptoms. It is important to rate each symptom for severity and frequency, and to operationalize criteria to meet the case definition. Using the question: "how much does this symptom bother you," for a symptom to meet criteria, it should be rated a 4 or higher on the following scale: 1 = no problem, 4 = moderate problem, 7 = big problem. In regard to how often the child has the symptom, to meet criterion, a symptom would have to be rated a 4 or higher on the following scale: 1 = hardly ever, to 4 = half of the time, to 7 = always.

*Post-exertional malaise and/or post-exertional fatigue.* With activity (it need not be strenuous and may include walking up a flight of stairs, or as minimal as using a computer or reading a book), there must be a loss of physical or mental stamina, rapid/sudden muscle or cognitive fatigability, post-exertional malaise and/or fatigue and a tendency for other associated symptoms within the patient's cluster of symptoms to worsen. The recovery is slow, often taking 24 hours or longer.

*Unrefreshing sleep or disturbance of sleep quantity or rhythm disturbance.* These symptoms may include prolonged sleep (including frequent naps), disturbed sleep (e.g. inability to fall asleep or early awakening), and/or day/night reversal.

*Pain (or discomfort).* These symptoms are often widespread and migratory in nature. There needs to occur at least one symptom from any of the following: Myofascial and/or joint pain, abdominal and/or head pain. Myofascial pain can include deep pain, muscle twitches, or achy and sore muscles. Pain, stiffness, or tenderness may occur in any joint but must be present in more than one joint and lacking edema or other signs of inflammation. Children with abdominal and/or head pain may experience eye pain/sensitivity to bright light, stomach pain, nausea, vomiting, or chest pain. People with ME/CFS often describe headaches as localized behind the eyes or in the back of the head, and may include headaches localized elsewhere, including migraines.

The young people must also experience two or more neurocognitive manifestations, which can include: impaired memory (self-reported or observable disturbance in ability to recall information or events on a short-term basis), difficulty focusing (disturbed concentration may impair ability to remain on task, to screen out extraneous/excessive stimuli in a classroom, or to focus on reading, computer/work activity, or television programs), difficulty finding the right word, frequently forgetting what one wanted to say, absent mindedness, slowness of thought, difficulty recalling information, need to focus on one thing at a time, trouble expressing thought, difficulty comprehending information, frequently losing train of thought, or new trouble with math or other educational subjects.

Finally, the child must experience at least one symptom from two of the following three categories: 1. Autonomic manifestations: Neurally mediated hypotension, postural orthostatic tachycardia, delayed postural hypotension, palpitations with or without cardiac arrhythmias, dizziness, feeling unsteady on the feet—disturbed balance, shortness of breath. 2. Neuroendocrine manifestations: Recurrent feelings of feverishness and cold extremities, subnormal body temperature and marked diurnal fluctuations, sweating episodes, intolerance of extremes of heat and cold, marked weight change-loss of appetite or abnormal appetite, worsening of

symptoms with stress. 3. Immune manifestations: Recurrent flu-like symptoms, non-exudative sore or scratchy throat, repeated fevers and sweats, lymph nodes tender to palpitation—generally minimal swelling noted, new sensitivities to food, odors, or chemicals.

### Severe versus moderate categories

We created a separate category for those who met almost all criteria, and they were classified with the Moderate ME/CFS Clinical criteria. These adolescents needed to have 3 or more months of fatigue and needed to report four out of the five classic ME/CFS symptoms with frequency and severity ratings of moderate or severe (a rating of 4 or higher, on a scale of 1–7). In addition, for autonomic, neuroendocrine, and immune manifestations, adolescents had to have at least one symptom in any of these three categories, as opposed to one symptom from two of the three categories.

### Other categories

The Pediatric Case Definition for ME/CFS also diagnoses children and adolescents with subtype variations of ME/CFS for those who experience idiopathic chronic fatigue. One subtype variation is Atypical ME/CFS, which is defined as 3 or more months of fatigue, but missing more than one classic ME/CFS symptoms. It is also possible to receive a diagnosis of ME/CFS in remission, if they met full symptom criteria at one time but were not experiencing full symptomology at the time of the study. Another category involves Pediatric ME/CFS-like illness, which is defined as meeting all classic ME/CFS symptom criteria, except for the 3 month duration or when one is lacking a medical evaluation.

### Exclusionary conditions

Exclusionary conditions include any active medical condition that may explain the presence of chronic fatigue, such as: untreated hypothyroidism, sleep apnea, narcolepsy, malignancies, leukemia, unresolved hepatitis, multiple sclerosis, juvenile rheumatoid arthritis, lupus erythematosus, HIV/AIDS, severe obesity (BMI greater than 40), celiac disease, and Lyme disease.

Other exclusionary illnesses include some active psychiatric conditions that may explain the

presence of chronic fatigue, such as: childhood schizophrenia or psychotic disorders, bipolar disorder, melancholic depressive disorder, active alcohol or substance abuse—except alcohol or substance abuse that has been successfully treated and resolved should not be considered exclusionary; active anorexia nervosa or bulimia nervosa (eating disorders that have been treated and resolved should not be considered exclusionary).

### Non-exclusionary disorders

The child may have the presence of concomitant disorders that do not adequately explain fatigue, and are, therefore, not necessarily exclusionary. These include psychiatric diagnoses such as: school phobia, separation anxiety, anxiety disorders, somatoform disorders, and non-melancholic depressive disorders; other conditions defined primarily by symptoms that cannot be confirmed by diagnostic laboratory tests, such as: multiple food and/or chemical sensitivity, fibromyalgia; any condition under specific treatment sufficient to alleviate all symptoms related to that condition and for which the adequacy of treatment has been documented; any condition that was treated with definitive therapy before development of chronic symptomatic sequelae; and any isolated and unexplained physical examination, laboratory or imaging test abnormality that is insufficient to strongly suggest the existence of an exclusionary condition.

### Conclusion

According to the new Pediatric case definition, the following six classic categories include fatigue, post-exertional malaise; unrefreshing sleep, or disturbance of sleep quantity or rhythm; myofascial pain, joint pain, abdominal and/or head pain; two or more neurocognitive manifestations, and at least one symptom from two of three subcategories including autonomic manifestations, neuroendocrine manifestations or immune manifestations. This new case definition and assessment instrument will facilitate future research on pediatric ME/CFS and long term investigations into outcomes of the illness, helping to identify risk factors which may predict prognosis.

Many clinicians are faced with children who have unexplained fatigue and other symptoms for which exhaustive medical and psychosocial evaluations have not revealed an acceptable

explanation. For any child with a chronic illness, an ongoing diagnostic evaluation that involves looking for either primary causes of fatigue and other symptoms or complications of underlying processes, is essential (Carter and Marshall, 1995). A case definition is the critical beginning step in the diagnostic process. If the illness category is overly inclusive and leads to the inclusion of many who do not have this illness or does not include some with the illness, then this will make it more difficult to ultimately find biological markers for this illness and to better understand the pathophysiology of this illness.

Having a pediatric case definition is a critical first step for both the diagnostic effort and subsequently will impact the types of interventions that are developed for those with this illness. Investigators have an important role to play in now using this international case definition to identify cases, investigate prevalence estimates, and study the pathophysiology of children and adolescents with this illness. In addition, this new case definition can be referenced by pediatricians, legislators, researchers, school nurses and even school teachers and staff responsible for developing and implementing Individual Education Plans. In addition to the diagnostic and educational benefits, the criteria can also be useful to the families dealing with pediatric ME/CFS, providing a mechanism to lend legitimacy to the child's symptoms.

### Disclosure

The authors report no conflicts of interest.

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