

Key Aspects of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) in Children and Adolescents

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Thank you for the opportunity to provide further information on pediatric ME/CFS.

OVERVIEW

We will cover the following:

- What is "ME" and what is "CFS" ?
- Prevalence in children and adolescents
- Pathophysiology
- Possible causes
- Diagnosis
- Key symptoms and signs
- The character and quality of life for young people with this illness and their families
- What ME/CFS is not
- Management/ treatment
- Role of school nurses and great importance of school participation in management
- Prognosis
- TAKE HOME POINTS

What is "ME/CFS"?

The Centers for Disease Control and Prevention (CDC) recognizes CFS as "a debilitating and complex disorder characterized by profound fatigue that is not improved by bed rest and that may be worsened by physical or mental activity. Symptoms affect several body systems and may include weakness, muscle pain, impaired memory and/or mental concentration, and insomnia, which can result in

reduced participation in daily activities.” Children and adolescents may have additional symptoms not seen as frequently in adults, such as abdominal pain, dizziness and inability to stand or sit.⁽¹⁾

For the last 60 years there has been a raging battle about the nature of this illness and whether it was a medical or psychological illness. On a scientific basis, the war is over. It is now absolutely clear that ME/CFS is a medical illness, and not psychologically caused.⁽²⁾

The terms “Myalgic Encephalopathy” or “Myalgic Encephalomyelitis” and “ME” were coined by some British physicians in the 1950’s who described a serious multisystemic illness that appeared among large clusters of hospital personnel. In the years following the outbreak in England a group of British psychiatrists decided that ME was a psychologically caused illness. They were totally wrong. They based their conclusions on very flawed research design and techniques but their many errors have plagued and continue to plague patients throughout the world.

Thirty years after the outbreak in the UK there were similar outbreaks in the Lake Tahoe area along the Nevada/California border as well as in upper New York State. The local physicians caring for patients also encountered a very serious multisystemic illness, not seen previously. The local physicians, now famous and still “on the case” were and are in no doubt that what they were seeing was an organic medical illness.

The CDC was called in to investigate the Lake Tahoe outbreak. From the beginning the CDC team believed it was all hysteria, not a real illness. They made no connections with the British experience. While the term they and outside advisors later devised, Chronic Fatigue Syndrome or CFS, seemed free from any bias, such was not the case within the CDC. Indeed, for many years, their consultants were the British psychiatrists who like their earlier colleagues, promulgated the myth of psychological causation. It is only in the last year that the CDC has begun to recognize and address their errors.⁽³⁾

The negative effects of belief in psychological causation have been many. For over 20 years millions of dollars were wasted on flawed behavioral studies, while needed biological research was stifled, interested researchers were not funded, and clinicians who recognized the medical nature of the illness reported by their patients, children and adults, were looked down upon by their colleagues.

Nevertheless, key biological research was gradually done in key parts of the world, and researchers and clinicians have coordinated their efforts. Many of the biological mysteries have been illuminated although much remains to be done. The World Health Organization recognizes this illness as a neurological disorder.⁽⁴⁾

In very recent years researchers here and in other countries have recognized the similarity of ME and CFS so that a temporary designating term, ME/CFS, is now being utilized.⁽²⁾

Prevalence

ME/CFS affects females 3 to 4 times more often than males. The prevalence rate in adults is 0.42 %.⁽²⁾ Epidemiological research has been less robust for children than for adults so the prevalence rates are less solid, but it is estimated that 0.1 to 0.3% of children and adolescents suffer from the illness.⁽⁵⁾ It is less common in children under 10.⁽⁶⁾ In young children it is likely to have a gradual onset, while adolescents are more likely to have an acute onset.

Prevalence rates translate to 27,000 adults in Massachusetts with ME/CFS and about a million in the USA, most of them undiagnosed. For kids, rates translate to somewhere between 7,000 and 20,000 in Massachusetts alone. Again most of these children go undiagnosed or misdiagnosed.

ME/CFS is more common than juvenile diabetes and many other chronic childhood illnesses.⁽¹⁾ ME/CFS is said by some researchers to be the most, or among the most, common causes of prolonged school absence.⁽⁷⁾ It is likely, therefore, that you will encounter at some time in your career, children who have ME/CFS, whether diagnosed or not.

Pathophysiology, or, what goes wrong?

Although there are significant gaps, much is now known about what goes wrong in patients with ME/CFS.⁽²⁾

- There are many significant abnormalities in *immune system* functioning, for example, dysfunctional and ineffective natural killer cells.
- There are also multiple *neuroendocrine* dysregulations.
- As demonstrated by functional MRI studies, EEGs, laboratory studies of cerebral spinal fluid, there are many *abnormalities in the brain* correlating with the type and degree of illness symptoms.
- Connected with these brain abnormalities are *multiple impairments of cognitive functioning* including:
 - Limited executive functioning
 - Slowing down of factual processing and learning of new information
 - Impaired working memory
 - Decreased concentration and attention span
 - Problems with word retrieval, etc.
- Physical and cognitive exertions can markedly worsen symptoms.
- *Energy metabolism* is seriously impaired, from the level of dysfunctional cellular mitochondria to the level of abnormal aerobic metabolism. The “fatigue” aspect of CFS is a matter of malfunctioning of key bodily mechanisms. The fatigue experienced is not simple tiredness but rather a state of profound exhaustion.
- *Autonomic dysfunction and abnormal cardiovascular function* are very real impairments. The incidence of orthostatic intolerance, manifested as neurally mediated hypotension (NMH) and/or postural orthostatic tachycardia (POTS) is higher in children and adolescents than in adults.
- In addition there is strong evidence that *genetic factors* play a role in susceptibility to ME/CFS. It is now clear that in ME/CFS the *expression of certain genes* is altered affecting immune modulation, oxidative stress, apoptosis.

The bottom line is that we now know a great deal about impairments in ME/CFS. It seems now, with the pace of research picking up globally, that each month another piece of the puzzle is clarified.

Possible Causes

As just mentioned, some people are genetically more vulnerable to becoming ill with ME/CFS. *Causal* factors considered to be important include *infectious agents*—viral, possibly retroviral, and possibly bacterial—and *environmental toxins*, all taking a toll on the immune system.⁽²⁾

Kathy Rowe at Royal Children’s Hospital in Australia and others highlight the significance in children and adolescents of preceding infectious mononucleosis after which a post-viral fatigue syndrome morphs into ME/CFS.⁽⁸⁾ A community-based study done in Chicago reported that 13% of adolescents with infectious mononucleosis met the criteria for ME/CFS six months later.⁽⁹⁾ Conversely, in Rowe’s study 60% of children and adolescents with ME/CFS reported a history of mononucleosis. So clearly, having mono is a risk factor for ME/CFS in young people.

We might ask, why hasn’t a specific agent been detected? The hypothesis is that an infectious agent “hits” the immune system causing a cascade of pathological events, then “runs” or disappears so that the agent itself is not detectable later, although there may be immunological evidence of its former presence. Whatever the causal trigger, the nature and toll of the pathophysiological cascade that results share common characteristics.

Diagnosis

A problem plaguing all research and clinical diagnosis to date has been the use of differing criteria for what constitutes ME/CFS. For example several criteria-sets, including those used by the CDC until very recently and those used by some British researchers, were so broad and/or vague in what was included that people with

primary psychiatric problems were lumped in. This has led to totally erroneous conclusions about the incidence of psychiatric causation of ME/CFS.

Fortunately there are much better diagnostic criteria available now both for adults and for children. These criteria, or illness definitions, were pioneered by the Canadian Dr. Bruce Carruthers and by Leonard Jason in the United States.^(10,11) ME/CFS in children and adolescents is different in some important ways compared with adults, so the criteria are somewhat different. The older the adolescent, the more the illness presents like the adult symptom profile.

Diagnosis is not complicated, but it can be a lengthy process. We will spend a little time on it because very few pediatricians are knowledgeable about this illness, and because of this it may take several years for a young person to get an accurate diagnosis. Many children and adolescents remain undiagnosed or misdiagnosed. Without an accurate diagnosis, it is much more difficult for the child and family to get the support they desperately need from the school, or even good management and treatments from the medical community.

The details of the pediatric diagnostic criteria are included in your conference binder and are also on the Resource CD.⁽¹¹⁾ A key point, for both youth and adults, is that there is as yet no generally accepted definitive biomarker or laboratory test. There are many possible biomarkers being investigated but there are none which are universally accepted at this time.

Diagnosis is based on excluding other possible causes of the array of symptoms, plus finding a fairly typical set of signs and symptoms. The primary healthcare provider must take a very careful medical history, developmental history, family and social history and do an equally thorough physical exam. Both parents should be interviewed during the evaluation as well as the child/adolescent. This part of the evaluation takes at least an hour. If only twenty minutes is allowed it is unlikely that an accurate diagnosis can be made unless follow up visits are possible to complete the evaluation.

Standard laboratory tests should be obtained. Although the results for ME/CFS patients are usually normal⁽²⁾, these tests can help rule out other illnesses. There are specialized tests that can help but these are expensive and available only in tertiary health care facilities.

In the past, pediatric criteria called for symptoms being present for at least 3 months (vs. 6 months in adults) before making a diagnosis of ME/CFS but such arbitrary limits are now being questioned. The sooner the diagnosis is made the sooner a treatment plan can be devised and implemented. Much research indicates that the sooner treatment is begun the higher the likelihood of a better outcome.

Symptoms

The pattern of symptoms follows from the pathophysiology we covered earlier. Among the typical symptoms are the following:^(2,7,11)

- *fatigue* that often is more like profound exhaustion than simply being tired;
- *fluctuating energy levels*;
- *sleep disturbances* with sleep being unrefreshing and leading to problems of sleep deprivation;
- *hypersensitivity to light and sound*;
- *widespread pain in muscles and joints*;
- *abdominal pain*;
- *headaches of a new type never before experienced*;
- *multiple cognitive difficulties* (impaired memory, confusion at times or “brain fog”, slowed comprehension, difficulty concentrating, word finding difficulties, etc.) that make learning very challenging;
- *autonomic problems*, more common in children than adults, demonstrated by neurally mediated hypotension or NMH, postural hypotension, postural orthostatic tachycardia, shortness of breath, disturbed balance;
- *neuro-endocrine symptoms* including intolerance of heat or cold, low body temperature, yet with a feeling of feverishness;

- *immune system manifestations* such as recurrent flu-like symptoms, sore throat, tender lymph nodes, new sensitivities to foods, medicines, or chemicals.

A key symptom in children and adults is what is known variously as post exertional malaise or PEM, or exercise intolerance.⁽¹²⁾ Young people and adults with ME/CFS have low thresholds for exertion and require a much longer time for recovery than is the case for healthy people. The exertions that can trigger a collapse lasting for 24 hours or more can be either physical or cognitive efforts as simple as climbing a flight of stairs or reading a book.

These symptoms fluctuate in severity over time, and over time some symptoms may abate and new symptoms appear. This pattern is very puzzling to the young patient, family, doctor and school officials, but is quite typical of ME/CFS.

While psychological factors are not causative young patients with ME/CFS may exhibit anxiety and a depressed affect secondary to the monumental changes in their lives, including fear about what is happening to them, the loss of the capacity to maintain their previous functional status, inability to keep up with their peers in school and in their social life, and dealing with skeptical and sometimes suspicious professional authorities at school and in the medical setting.

Signs

It was thought until recently that there are no significant *signs*, that is, objective findings found in pediatric ME/CFS patients on physical exam, but according to Peter Rowe, a pediatrician at Johns Hopkins, there are important signs which may be present.⁽⁷⁾ These include:

- elevated heart rate,
- abnormal blood pressure and heart rate on prolonged standing or upright position,
- “dependent acrocyanosis” (purple discoloration) in the lower portions of the legs, and

- presence of hypermobility of the joints.

Many clinicians believe that diagnosis of ME/CFS in children and adults is difficult. Perhaps, but given sufficient knowledge of the illness, adequate time, a thorough evaluation and opportunity to observe the child over time, it is my opinion and experience that an accurate diagnosis can be made. However, one or more specific biomarkers would certainly help. As one teen we know wrote in a poem, having purple polka dots would help.

What ME/CFS is not and issues of the quality of life

ME/CFS is **not** school phobia: young people with ME/CFS want to go to school and want to keep up with their studies. They will often choose to attend school to the detriment of their physical condition.

ME/CFS is **not** a form of a psychosomatic disorder or a form of malingering. Simply getting to know the child and family can help distinguish ME/CFS from such an entity.

And ME/CFS is **not** Munchausen-by-proxy. Misdiagnosis and wrongful accusations by uninformed healthcare professionals and school authorities have caused great harm to many children and their beleaguered parents. We have seen such situations all around New England. They result from ignorance of the healthcare providers and other professionals. Educating them could avoid these terrible errors.⁽¹³⁾

Many people with ME/CFS “look fine” much of the time and are trying their very best to “act fine”, yet are severely impaired. If they manage to do normal activities for a few hours, they may pay later with days in bed. They may feel OK one hour, and be desperately sick the next. It is crucial to believe the child, who does not want to be sick, in order to support them in doing the best that they can do.

As in adults there is a wide range of the impact of the illness on children and adolescents, from relatively mild to very severe with the child/adolescent confined

to bed or unable to leave the house. Most patients are somewhere in between, but the severity of symptoms can also fluctuate over time.

Because of all of the impairments in their functioning, most children and adolescents with ME/CFS have great difficulty in every aspect of their lives. Misdiagnosis and inappropriate treatments compound the many losses and stresses, causing a worsening of the illness. The toll on their families is major, as you have heard. As the illness usually continues for many years, the challenge of caring for these children can be very great.

Management/Treatment

While, at this point, there is no cure, there is much that can be done. Some of the specific symptoms can be alleviated to varying degrees, either by judicious use of medications or by other means.

The following symptoms are subject to treatment with appropriate *medications*:

- sleep abnormalities,
- pain, and
- autonomic problems.

Details about medication are contained in the IACFS/ME Primer which is on your Resource CD.

There are two simple rules about the use of any medication in children and adults with ME/CFS:

1. Initial doses must be started at well below usual dosages and raised very slowly and gradually if at all.
2. Medications must be monitored closely, because of possible atypical responses in individuals with ME/CFS.

Non-medication strategies can help as well. They are as follows:

- Providing accurate information to the child and family about the nature of ME/CFS so they know what to expect and what can and can't be done. Inappropriate anxieties and fears should be addressed by the physician or other professional. This clarifying/learning process may take time.
- Learning to pace activities so as to be able to do what is feasible while not going beyond certain limits. Going beyond those limits can trigger post-exertional malaise and exacerbate many of the other symptoms.
- Children and adolescents often tend to overdo as they try to keep up with their peers. When they can't do so they begin to become socially isolated. Parents and others need to address that isolation.
- Often uninformed clinicians advise exercise programs such as "GET" or Graded Exercise Therapy. AVOID THESE LIKE THE PLAGUE!!! They inevitably exceed appropriate exercise limits unless carried out by a well-trained physical therapist knowledgeable about ME/CFS and who follows guidelines established by exercise physiologists.
- Of course the challenges of continuing to learn academically are huge—and it is hugely important to a successful outcome for the child.⁽⁸⁾

The importance of schools and particularly school nurses

Children and adolescents with ME/CFS, as you have heard, want to go to school, want to continue their education, but they may need much help over a period of years in order to do so. Research has shown that ongoing support particularly in navigating the education system was an essential contributor to the quality of life and ability to cope. Similarly the stories that you have heard today attest to the great importance of a close cooperative relationship with school personnel.

It is clear that the school nurse is a key person in working with the family and child, and in educating other school personnel about the nature of ME/CFS. School personnel need to know about the variability in energy levels, cognitive limitations, the need for an individualized and flexible educational plan, and the need for a safe supportive environment at school.

There are other specific ways school nurses can help, such as:

- being aware of what medications a student with ME/CFS is on and noting possible side effects;
- suggesting appropriate accommodations for a 504 plan; and
- believing the student when they need help during the school day.

Other school personnel such as guidance counselors, teachers and principals can help a lot in devising educational plans, but **only** if they are well informed about the medical nature of ME/CFS in kids and the characteristics of the illness. Having to counter skepticism or outright opposition from school administration and teachers adds great strain to parents and young people already dealing with a severe and frightening physical illness.

Prognosis

Some researchers have reported that the prognosis for children and adolescents with ME/CFS is better than for adults. Kathy Rowe has done a major follow up study on a large number of kids seen and treated at her hospital clinic. With the best of care, by 5 years, 60% reported recovery and by 12 years 88% reported recovery⁽⁸⁾. Peter Rowe at Johns Hopkins reported that, with coordinated and knowledgeable care over a period of years, many children in his clinic experienced significant improvement. However, these are isolated and specialized centers, and most young people with ME/CFS do not have this opportunity. Peter Rowe reported recently that the quality of care available to most children with ME/CFS has not improved at all in the last 7 years, at the same time that we have come to understand a great deal more about the illness.⁽⁷⁾

There is agreement that early diagnosis and high quality treatment and management over several years or longer increases not only chances for recovery for kids but also their quality of life.

The biggest barrier to providing good care is ignorance and lack of understanding on the part of health care professionals, school personnel and families. This is something that can be effectively addressed, with your help, for one child at a time.

Take home points

- ME/CFS is an often severe medical illness in a significant number of children and adolescents. Often more than one child in a family is affected.
- It is not a psychological illness.
- Viral and chemical insults are likely to be among the causes but much more research is needed.
- Many of the abnormalities in bodily functioning are now known and help explain many of the symptoms.
- The range of illness impact varies from mild to very severe, and symptoms may fluctuate.
- There is currently no cure, but there is much that can be done to relieve some of the symptoms, including use of medications and non-medication tactics.
- The possibility of significant improvement in the pediatric age group is increased with good treatment and management, but “recovery” is usually a matter of years, not months.
- Unfortunately most health care professionals are poorly informed or misinformed about ME/CFS.
- Education of medical and school professionals is key to recognition and management of young people with ME/CFS.
- School nurses have a vital role in the management of pediatric ME/CFS.

Thank you.

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