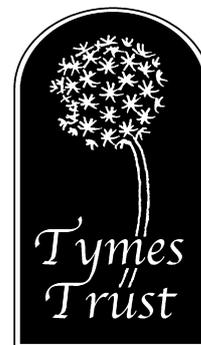


# *Professional Guides*

## **The Doctor's Guide to ME in Children and Young People**

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### **Abstract**

*This Guide concerns the recognition and management of this condition in children and young people. Primarily intended for Paediatricians and General Practitioners, but may also be useful to nurses, physiotherapists and other medical professionals.*

*The Department of Health now refers to this condition as CFS/ME*

Many doctors use the term CFS (Chronic Fatigue Syndrome). Others prefer ME (Myalgic Encephalomyelitis) as originated in The Lancet.

This guidance concerns the neurological condition classified under the names ME and CFS by the World Health Organisation as a disease of the brain and nervous system (ICD 10; G93.3).

# ME in Children and Young People

*For many years Dr Alan Franklin was the country's foremost specialist in childhood ME. Unfortunately he is no longer with us, but we still know of no better practical guide to supporting these patients.*

## 1 Introduction

The existence of ME as an organic illness dates back as long as records have been kept. It is now recognised in people of all ages, including children. The effect that this neurological disability can have can be quite devastating for the lives of young people. It must be taken seriously if children and students are to be given maximum help to recover some of their lost opportunities.

## 2 Historical

2.1 Myalgic Encephalomyelitis (also known as Chronic Fatigue Syndrome and formerly called Atypical Polio) is a serious neurological illness (WHO ICD 10; G93.3). An illness with clinical features of muscle pain, neurocognitive problems and exercise-induced fatigue has existed for centuries. In the 20<sup>th</sup> century, epidemic outbreaks were recorded from 1934 until the 1950s. Earlier names included 'English sweats', 'epidemic neuromyesthesia', and 'atypical polio'. The term Myalgic Encephalomyelitis (ME) first appeared in the Lancet (Acheson 1956). Clinical features were documented (Ramsay 1986) following a series of world-wide outbreaks. ME has been well documented in children and young people [1].

2.2 The validity of the term 'Myalgic Encephalomyelitis' has been disputed because not all cases suffer muscle pain (myalgia) nor is there always evidence of swelling of the spinal cord with long tract neurological signs (myelitis) but it is an encephalopathic illness because the symptom complex cannot be attributed to lesions at any other level. This would include headaches, central fatigue, photophobia, phonophobia, cognitive impairment, sleep disturbance etc. In addition, objective measurements of brain function such as electroencephalography and measurements of blood flow have shown clear abnormalities. Recent research shows evidence of inflammation.

## 3 Pathogenesis of the Illness

3.1 There is still uncertainty about the patho-aetiology of ME and CFS. Studies have suggested that viruses may initiate the response (Komaroff 1996). Clinically there are similarities between post-polio syndrome and ME/CFS (Bruno 1996) suggesting a common response to specific enterovirus infection. In some patients there is

reduced circulating blood volume, which contributes to the postural hypotension (dizziness and confusion when upright) so frequently experienced (Streeten and Bell 1997).

Low dose chemical exposure is known to have a damaging effect on the central nervous system and ME is clinically similar to illnesses resulting from known organophosphate exposure (Behan 1997) and to Gulf War illness (Jamal 1996). Publicity has been given to the possible contribution of OP poisoning to onset of ME in children who have been treated for head lice using a pesticidal anti-lice shampoo containing OPs [1].

3.2 Most illnesses appear to start after an acute febrile illness, or very occasionally after an immunisation. Either a micro-organism or more likely antibody titre of significance, can be found in up to 50% of cases [2].

However, in some cases there is a gradual onset with no clear starting event and Scottish researchers have found that previously damaged muscle is more readily invaded by viruses but they fail to disrupt the cells and persist. The neurological symptoms are not pathognomonic.

3.3 Some workers have suggested [3, 4] that ME could be an atypical form of poliomyelitis.

3.4 Dr JA Goldstein [5] has suggested that the infective agent codes for immunosuppressive substances and either that or micro-organisms upregulate the system so that excess cytokines are produced. Then more distant multiple organ systems are affected, leading to the multiple symptoms of ME. These later phases of the illness affect the immune exclusion system, the production of allergies, the function of the hypopituitary-adrenal axis and the multiple physical symptoms.

Other workers have suggested that the infecting virus interferes with cellular energy production via the mitochondria [6] or that viruses attack the 5 HT receptors in the brain stem [7] and switch on the HPA system so that glucocorticoids are elevated [8]. Some cytokines (eg Interleukin 1) cause a similar elevation. Receptors in the hypothalamus and limbic system are then switched off, leading to disturbances of appetite, sleep, mood and temperature regulation.

3.5 Typically, the illness runs a remitting and relapsing course over a period of years.

3.6 There may be a genetic predisposition, in view of the not uncommon occurrence of ME affecting more than one member of a family [1].

3.7 The *average* bout in teenagers lasts about four and a half years but the condition is potentially open-ended [9, 10]. In Rangel et al [10] (*The course of severe chronic fatigue syndrome in childhood*) 47% of the 'recovered group' were still suffering symptoms, as the researchers were at pains to point out. One third of the 'recovered group' were not at school full-time. Therefore 'recovered', in this context, does not imply 'totally fit'.

#### 4 Clinical presentation and diagnostic criteria

4.1 The government Chief Medical Officer's Working Group on CFS/ME developed new diagnostic criteria for children, but these were omitted from the published report [11]. The Fukuda 1994 diagnostic criteria for CFS in adults were defined chiefly for research purposes. Young patients may not always fulfil CFS criteria, and yet still have a typical clinical picture of ME/CFS. There are some clinical features in children that are different from those in adults, especially in children under 10 years of age. The onset is often more gradual in young children, and their daily behaviour is more variable, without a clear history of an initiating infection.

*[The Trust has issued a statement on the 2003 Canadian Definition of ME/CFS. In our opinion it is the best contemporary definition. It was developed for clinical practice and was compiled by physicians who have seen over 20,000 patients. We believe that under the Canadian Definition it is harder for people with 'chronic fatigue' to be misdiagnosed with ME/CFS.]*

Certain symptoms - intractable headache, abdominal pain, loss of appetite - are more common in children. There is no clinical difference, once the illness is established, between children whose onset is rapid, usually following an acute febrile episode, and those with a gradual onset, as is seen more often in young children.

The diagnosis is much more difficult in young children because they cannot articulate symptoms such as fatigue and cognitive difficulties. Parents and teachers need to observe and assess symptoms such as onset of pallor and exhaustion.

4.2 A marked feature of ME is the fluctuation of symptoms from day to day, and the tendency for relapses and remissions over months. There is a combination of key symptoms that is remarkably similar from patient to patient: ***Post-exertional fatigue, malaise and cognitive dysfunction are invariably present.*** It is important for medical

#### Common symptoms and signs [1]

- a) The commonest feature for diagnosis of ME is persistent ***fatigue***. This is better described as exhaustion, asthenia or weakness, which is usually ***post-exertional***, developing up to 3 days following moderate effort, and is not relieved by rest/sleep. The fatigue may appear as orthostatic intolerance<sup>1</sup> (dizziness or faintness when upright) rather than simple tiredness or sleepiness. The fatigue may be physical or mental, can be severe and often fluctuating, and leads to significant reduction in normal activities.
- b) Severe malaise (feeling 'poisoned'), particularly following physical or mental exertion.
- c) Persistent headache, not responding to painkillers.
- d) Disturbance of normal sleep pattern. Hypersomnolence is commonest initially, often progressing to sleep reversal, or else insomnia.
- e) Neurocognitive disturbance is invariably present (eg loss of attention, concentration, and short-term memory, forgetting names, inability to understand a written paragraph).<sup>2</sup>
- f) Visual disturbance (eye pain, blurring, especially when reading).
- g) Sensitivity to sound and/or light.<sup>3</sup>
- h) Recurrent sore throat and/or swollen glands (misleading in children, who develop them with every infection. Prolonged adenopathy may need investigation to exclude TB or malignancy).
- i) Muscle or joint pain, especially of lower back and lower limbs.
- j) Nausea, abdominal pain, loss of appetite.
- k) Balance disturbance, or dizziness on sudden change of position.
- l) Altered subjective temperature regulation (inappropriate sensations of fevers or chills, night sweats), and maybe objective reversal of sleep/temperature rhythms.
- m) Facial pallor, especially with the onset of severe fatigue (Ramsay 1986).
- n) Altered skin sensitivity, paraesthesiae (numbness, tingling), transient rash.
- o) Mood changes (irritability, depression, anger and frustration) that are out of character.

<sup>1</sup> Measured by recording blood pressure recumbent, then at 5 minute intervals standing still. In health, blood and pulse pressures can be maintained while standing for at least 1 hour.

<sup>2</sup> This disturbance of neurocognitive function can cause acute distress to adolescents who are usually keen to return to school, but find they are unable to function normally. It is not appropriate to return a child to school immediately, without further educational assessment. That this disturbance is part of the illness and not due to psychiatric co-morbidity has been confirmed by Deluca and colleagues (Deluca 1997).

<sup>3</sup> These are part of the great difficulty children with ME have in coping with normal input - whether cognitive, visual, aural or visceral - because of rapid brain fatigue.

professionals to recognise the multiplicity of symptoms that commonly occur, as well as 'fatigue'.

**4.3 *The more severe forms of the illness in children and adolescents*** include symptoms such as dizziness, unremitting headache, severe muscle spasms that may require splinting to prevent contractures in the hands or feet, shaking episodes or pseudo-seizures without loss of consciousness, difficulty swallowing and paresis or paralysis of limbs, bladder irritability and a disturbed mental state.

4.4 Typically, physical exhaustion comes on within 12 hours of minimal exertion, taking more than 24 hours to recover. Fatigue following cognitive effort may be delayed up to 2 days and last even longer and give rise to similar physical exhaustion. It is notable that the child does not generally suffer loss of motivation.

4.5 The child is likely to wake from sleep feeling exhausted and to suffer a disturbed sleep pattern. Nightmares and hallucinations occur in the more severely affected.

4.6 The illness can be intensified by any further intercurrent infection (eg common cold, sore throat) or by any unusual effort.

4.7 Many, if not most, of these symptoms may occur after any significant viral illness but they usually settle within a few days. In ME they persist almost daily for weeks extending to months or years and are found characteristically in enteroviral infections which nearly all children get annually. Again 90-95% of these enteroviral infections are asymptomatic. The symptomatic ones are typically biphasic with mild to moderate fever lasting a few days followed by apparent recovery then a secondary viraemia with widespread symptoms, which like polio include neurological symptoms which are infinitely variable from mild to severe including progressive paralysis in rare instances.

4.8 Many patients demonstrate particular language difficulties, including communication on more than a 1-to-1 basis and word-finding. Aphonia and dysphagia are particularly severe and distressing symptoms sometimes associated with atonia tremors and unusual clonic movements can occur which can easily be mistaken for hysterical conversion behaviour.

4.9 Breathlessness and breathing difficulties can occur.

4.10 Parents and teachers frequently report that the affected child when tired looks transparently pale and ill. One mother actually thought her child was dead!

4.11 Between bouts of exhaustion some children may be able to perform virtually normally for short periods of time and therefore appear to be quite well. But this effort cannot be sustained for very long and if they are only seen at such times may mistakenly be accused of 'having nothing wrong at all' or thought to have school phobia. Characteristically, energy levels fluctuate from day to day and during a single day.

## **5 Differential diagnoses**

5.1 Investigations should be mainly directed to exclude other known disorders eg thyroid disease, liver disorders, Lyme disease, primary muscle disorders and psychosocial disorders such as family disruption, child abuse, anorexia nervosa, school phobia and anxiety / depressive disorders.

*[From the Chief Medical Officer's Working Group Report, Department of Health 2002:*

*Neither the fact of a child or young person having unexplained symptoms nor the exercising of selective choice about treatment or education constitutes evidence of abuse.*

*In cases of CFS/ME, evidence clearly suggestive of harm should be obtained before convening child protection conferences or initiating care proceedings in a family court.]*

5.2 It is quite common for children and adolescents to develop loss of appetite as a result of ME. This is frequently due to nausea and/or to muscle fatigue which affects chewing and swallowing. This loss of appetite and reduced intake is often confused with anorexia nervosa, especially in girls in early puberty. Anorexia nervosa is associated with a distorted body image, self-induced vomiting, progressive weight loss, and frequently abuse of laxatives [1].

5.3 Any chronic disease of this nature in a child is bound to cause considerable strain on the family. Some may benefit from counselling but *all* will benefit from appropriate support. Suicidal thoughts and ideas are not unknown in children. Genuine endogenous depression with feelings of guilt and worthlessness may be a premorbid condition and must be treated in parallel.

5.4 Phobic anxiety state, particularly school phobia, is associated with panic attacks and use of the avoidance response about the most feared situation. Symptoms associated with school phobia usually resolve during weekends and school holidays. This does not occur with ME whose symptoms may be worse at weekends and persist through school holidays. The main reason that the pupil is reluctant to go to school is because of rapid onset of fatigue,

myalgia, malaise and loss of concentration after a short time in class [1].

5.5 Somatization disorder may resemble ME in that the patient has multiple symptoms which cannot be explained by any known medical condition or by use of abusive substance or medications. In ME there is typically no secondary gain from having the symptoms, whereas this is a common feature with somatization. When evaluating the child's bodily symptoms, it is important to be aware that a child often cannot articulate about the condition, and may be stressed by the attitudes of others to the illness. In a few cases, somatization could be difficult to differentiate from ME and there may be hidden stresses; a child can be unwilling or unable to communicate about sources of anxiety.

A study in the US (Bell 1996) evaluated the symptoms, severity, social support and ways of coping in 69 adolescents with ME/CFS. The results showed nothing to suggest that ME is primarily a psychiatric or psychosomatic illness. Exposure to new stress increases the severity of the symptoms. The incidence of co-morbid psychiatric illness in ME patients under 20 years of age has not yet been formally established, but is probably present at the same incidence as in the general population [1].

## 6 Management

There is no specific medical treatment yet available for this condition although a number of measures have been recommended.

6.1 **Rest** is extremely important in the acute stage of the illness when there is evidence of active viral infection and possibly other provoking factors. Following the acute phase patients should be encouraged to pace themselves and live within their energy levels. The criteria for this is that either cognitive or physical activity should not produce prolonged after-effects ie for hours or days. Patients should be encouraged to pace their energy expenditure and to learn to remain well within their capacity without exacerbating symptoms. Patients should stop activities before provoking symptoms and evidence of tiring should be a definite signal to stop and rest. Except in the acutely ill, total bed rest should be avoided. However, in the severely ill, bed rest is not harmful and may be essential. Even sitting up may increase the severity of the symptoms.

Children, in less severe cases of the disease, may continue regular schooling where possible, avoiding PE, long journeys and excessive homework. A reduced number of hours and subjects taken for examinations may be necessary and good communication with the school authorities is of

paramount importance. Activity levels will naturally increase as the child's symptoms improve. Less severe cases can become more severe due to too little adaptation at first so early diagnosis is vital. Excessive activity can be harmful.

The correct recognition of this specific disease may in itself dispel a great deal of stress, both in the child and the family, and may enable them all to cope with it and allow local authorities to activate local supportive measures.

6.2 It should be noted that there are many lesser illnesses associated with fatigue and tiredness which are not true ME. They may be the aftermath of, for example, surgery or acute flu-like illnesses, glandular fever etc, or more long term illnesses such as diabetes, cancer, asthma, anorexia nervosa, an accident or emotional trauma such as abuse, bereavement or family disruption.

6.3 It is important to recognise these and other surrounding factors, including previous personality and performance in making a diagnosis. Occasionally, onset may be gradual and start at a very young age.

6.4 By the time that ME is usually considered it will often be too late to find the initial infection and most biochemical results will be unremarkable. CT and MRI scans may not detect any cerebral abnormality but SPECT scans [12, 13] and QEEG have shown functional abnormality. The diagnosis is clinical, but can bring great relief to the bewildered family when recognised.

6.5 The management strategy should therefore centre on the *degree of disability* including the cognitive / neurological aspects and be built around appropriate lifestyle adjustments and sufficient rest. **Pacing** life should be the key and remember that all work and no play make Jack a dull boy! So, *prioritise* activities on a daily basis and conserve energy wherever possible.

6.6 Some doctors have recommended graded exercise programmes but overworking a damaged or energy deficient muscle could cause more damage. Muscle wasting usually accompanies peripheral neuropathies but damage can also occur if the type II (anaerobic) fibres are overused in the presence of mitochondrial impairment - as in the post viral disease.

It is startling how little wasting is seen in young people with ME who also have an intact CNS even after prolonged bed rest and how quickly this is restored when they recover; **clinical experience shows that recovery is slow but spontaneous and does not require exercise programmes.**

There are some cases who experience spinal paralysis (paraplegia) or pseudo-bulbar paralysis, though this is not usually so profound as in poliomyelitis. Passive physiotherapy can help to maintain a healthy blood flow. However, over-zealous physiotherapy can cause active harm. It is possible to describe this illness in terms of three stages:

#### *Stage One - Toxic*

Patient feels ill all the time. Any attempt at exercise is *counter-productive*. As in all acute illnesses, a drastic reduction in cognitive activity (including education) is usually indicated. However, this need for reduction in activity will typically persist for far longer than in other illnesses and it is the biggest cause of long term sickness absence from school [14]. Stage One is more apparent in severe cases.

#### *Stage Two - Stabilisation*

Any *excess* activity causes relapse to stage one. Extreme caution needed. Patients may remain in this stage for years and progress may be very slow.

#### *Stage Three - Remission*

Activities can be gradually increased with confidence.

Each stage is of variable length in different patients and with time the patient may be able to identify which stage they are in.

Relapses may lead to reversion to an earlier stage. For children, close observation by the parent or carer will usually determine the stage. **Listen carefully to the child!**

Progressive exercise programmes are therefore inappropriate except in Stage Three. If applied too soon the muscles may be further damaged. The pace of recovery is normally slow - encourage the patient to stay within comfortable (non-fatiguing) limits whilst remembering that recovery should be patient-led. Cognitive activity should be introduced following the same general principles.

*[From the Chief Medical Officer's Working Group Report, Department of Health 2002:*

*Overall, there is wide variation in the duration of the illness, with some people recovering in less than two years, while others remain ill after several decades.*

*A minority of those with CFS/ME remain permanently severely disabled and dependent on others.]*

6.7 Symptoms should be tackled as seems appropriate, remembering that patients with ME are typically very sensitive to medication and may need lower doses.

6.7.1 Simple analgesics like paracetamol can be tried for head and skeletal pain but, in ME, pain is not easily relieved. In severe headaches Diamox SR has occasionally produced some relief.

6.7.2 Antacids are rarely helpful but ordinary peppermints or ginger can relieve discomfort.

6.7.3 Magnesium, either IM or orally, has been recommended for patients with this disorder, but the clinical trials have been contradictory [15]. Nutritional supplements have been found to help some patients.

6.7.4 Zinc and Vitamin C for recurrent infection and sometimes an enzyme found in Bee propolis for sore throats may be helpful.

6.7.5 Sensitivities / allergies can be a feature of this disorder or may precede it, but any use of exclusion and challenge diets and sometimes desensitisation (EPD) should be supervised by a specialist skilled in allergy treatment. Dairy foods and wheat are often not well tolerated.

6.7.6 Candidiasis may be treated by the use of anti-fungal antibiotics like Fluconazole and a suitable diet.

6.7.7 Some patients report that immunoglobulin injections or infusions have helped them.

6.7.8 Sleep disturbance sometimes responds to simple hypnotics or minimal doses of amitriptyline.

6.7.9 Anti-depressant drugs are not usually helpful and patients do appear to be very sensitive. They should only be prescribed by practitioners skilled in their use and in the management of this disorder, because rarely do these drugs seem to help children. Treatment should commence with minimal doses.

6.8 Some patients report that homeopathy and acupuncture have helped them but neither these nor any of the above measures can be confidently recommended for all. Some may be worth a short trial eg gentle massage may help with relaxation.

6.9 Patience, realistic optimism, encouragement and a paced, expectant lifestyle are the most productive attitudes.

6.10 Forced exercise, particularly any exercise producing a prolonged after-effect, can be counter productive and can be damaging. It can be instrumental in causing a deterioration, despite reports to the contrary [16].

Very rarely some children, who may become bed ridden for long periods of time, may lose the incentive to improve and need compassionate encouragement.

6.12 As with all sick children, immunisations and flu vaccines should be avoided as a general rule; the risk / benefit equation has to be borne in mind.

6.13 Families can easily feel abandoned by their medical advisers if they are not regularly visited, even if the doctor may feel helpless and powerless to offer a definitive treatment. The support is usually greatly appreciated.

*[Caution : intramuscular injection in the presence of enteroviral infection carries risk of paralysis [20].]*

## 7 Education

Jane Colby (a former headteacher, consultant for the education of children with ME and a member of the Chief Medical Officer's Working Group on CFS/ME) has written guidelines to help schools adapt to special educational needs of children with ME.

7.1 Children with less severe disease may be able to continue at school with reduced activity eg part-time attendance, no PE or sport, help with transport to or from the school. They typically experience mental fatigue leading to limited learning capacity.

7.2 Children with moderate functional disability are unlikely to be able to complete a full day in school and will need rest periods.

7.3 Some may only manage several short sessions a week in school. Work will need to be prioritised to concentrate effort on a few subjects, others being dropped so that the effort available may be given to complete a limited number of examination subjects.

7.4 More severely disabled children will need home tuition and/or distance learning facilities. As they improve, it may be possible over a considerable period of time to reintroduce them into school. The transition period will need to be carefully managed. Some children are better educated at home.

7.5 The most severely disabled will be unable to benefit from education at all due to reading or cognitive difficulties and the severity of the illness. Attempts should be made by the school to maintain friendly contact in whatever way seems appropriate - occasional brief visits, audio tapes, written letters, emails or telephone calls.

7.6 Although the special educational needs of all children with ME must be considered, formal assessment [17] may be appropriate for some, especially the more severely affected over long periods of time. *[A sick child's rights to suitable education are detailed in statutory guidance [18] but note that misinterpretation of this guidance [19] is common.]*

7.7 A multi-disciplinary and multi-agency approach can help to reach a consensus with the family and the community paediatrician may be able to facilitate this arrangement. Parents and the child will be involved in this process. It is however, very distressing to the family if the professionals involved cannot appreciate how genuinely disabled the child is and how frustrated they feel at being unable to participate in school, family and peer group activities. To be labelled 'school-phobic' at such a stage will only add insult to injury!

## 8 Conclusion

Myalgic Encephalomyelitis (chronic post-viral fatigue syndrome) is a chronic, neurological illness, a disabling condition of children and adults which causes acute distress, loss of schooling and social contact and major functional disability. It is being increasingly recognised in the school population and clusters occur in schools, families and communities. It can also appear in epidemic form; at least 20% of schools have cases [14]. It is more common in girls than boys and in adults who have close contact with small children who probably form the reservoir of infection. It is thought to be an abnormal immune response to an infecting agent (entero- or other virus). This illness needs to be diagnosed early and treated sympathetically, allowing adequate rest and adjustment of lifestyle (pacing) to promote optimum recovery until a definitive cure is found.

## The Young ME Sufferers Trust

The Trust, the longest running national organisation supporting children with ME/CFS and their families, now operates a Professionals Referral service.

Faced with a case, or a suspected case, of ME/CFS, doctors, teachers, social workers and other professionals can telephone the Trust to consult an ME/CFS expert who is also a fellow professional of their own standing.

Dr Nigel Hunt, GP and Eastern Deanery Associate Director says: "I am pleased to assist this service. GPs can find it hard to believe that ME/CFS can mimic a brain tumour or stroke. I have dealt with extremely severe cases."

The service can put professionals in touch with, among others, hospital consultants, paediatricians, educational consultants, social workers and examinations officers, all with expertise in ME.

The Trust played a major role in the Chief Medical Officer's Working Group on CFS/ME and its Report (DOH 2002). The Trust is endorsed by the Prime Minister, the Leader of the Opposition and the Leader of the Liberal Democrats.

## References

- [1] Colby J, Franklin AJ, Macintyre A et al (1999) *Childhood ME* <http://www.youngactiononline.com/docs/chldhdme.htm>
- [2] Dowsett EG et al (1992) *Myalgic encephalomyelitis - a persistent enteroviral infection?* The Clinical and Scientific Basis of ME and CFS. The Nightingale Research Foundation, Canada pp285-291
- [3] Behan PO (1991) *The first Melvin Ramsay Memorial Lecture* Journal of Psych Med 1994
- [4] Hyde BM et al (1992) *The Clinical and Scientific Basis of ME and CFS* The Nightingale Research Foundation, Canada
- [5] Goldstein JA (1989) CFIDS Chronicle, Charlotte NC Jan/Feb 1989 p33
- [6] Behan WMH, Behan PO, More IAR (1991) *Mitochondrial abnormalities in the post viral fatigue syndrome* Acta Neuropathologica 83:62-65
- [7] Dinan E (1992) *The second Melvin Ramsay Memorial Lecture*
- [8] Demitrack MA (1991) *Evidence for impaired activation of the hypothalamus-pituitary-adrenal axis in patients with chronic fatigue syndrome* J Clin Endocr and Metabolism 73:1224-1234
- [9] Dowsett EG et al (1990) *Myalgic encephalomyelitis - a persistent enteroviral infection* Postgraduate Medical Journal 66:526-530
- [10] Rangel L, Garralda ME, Levin M, Roberts H (2000) *The course of severe chronic fatigue syndrome in childhood* Journal RSM vol 93 March 2000
- [11] *Chief Medical Officer's CFS/ME Working Group Report* Department of Health 2002 chapter 5 pp57-66
- [12] Costa DC et al (1992) *Brain stem defects in Myalgic encephalomyelitis* Letter in BMJ 304:1567
- [13] Costa DC, Brostoff J, Douli V, Ell PJ (1992) *Brain stem hypoperfusion in patients with ME/CFS* European Journal of Nuclear Medicine 19:733
- [14] Dowsett EG, Colby J (1997) *Long-term Sickness Absence due to ME/CFS in UK Schools* Journal of Chronic Fatigue Syndrome 1997 vol 3(2) pp 29-42
- [15] Cox IM et al (1991) *Red blood cell magnesium and Chronic Fatigue Syndrome* Lancet 337:757-760
- [16] Vereker ME (1992) *Chronic fatigue syndrome - a joint paediatric psychiatric approach* Arch Dis Child 67 no 4 550-555
- [17] *Code of Practice for the Identification and Assessment of Pupils with Special Educational Needs* Department for Education and Skills
- [18] *Access to Education for Children and Young People with Medical Needs* Department for Education and Skills 2002
- [19] Colby J (2003) *Back to school?* Special Children, Questions Publishing April/May 2003 pp 28-31 (also <http://www.tymestrust.org/pdfs/backtoschool.pdf>)
- [20] Deivanayagam N, Nedunchelian K, Ahamed SS et al *Intramuscular injection as a provoking factor for paralysis in acute poliomyelitis. A case control study.* Indian Pediatr 1993 Mar; 30(3):335-40