MYALGIC ENCEPHALOMYELITIS IN CHILDHOOD

How the Paediatrician Can Help

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I am a paediatrician based in County Durham who has seen approximately 200 children with ME in my local area over the last 20 years, as well as a further c2000 from outside the area. Most of my cases are teenagers but I have a handful of quite severe cases in the 5-10 age group. I have seen two cases where the onset appeared to be before the age of two.

Research has consistently shown that ME, also (misleadingly) referred to as 'chronic fatigue syndrome', has a major negative impact on the quality of life of patients young and old. By making a diagnosis and offering appropriate management and support we can improve the quality of life of young ME patients.

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IMPORTANCE OF DIAGNOSIS

First and foremost it is important to positively establish an accurate diagnosis. It is vital that a proper history is taken and that sufficient time is allocated for this task. Only then will the distinctive clinical picture that permits a positive diagnosis of ME be uncovered. The commonest reason for missing the diagnosis is to concentrate on one symptom only, or to take an incomplete history.

Clear and simple guidance on diagnosis is set out in the 2021 NICE Guideline: https://www.nice.org.uk/guidance/NG206

While 'fatigue' is commonly accepted as a key symptom, what ME patients experience is better described as **reduced energy levels**, together with **'fatiguability'**.

All symptoms can be made worse by physical exertion and mental effort can also make physical symptoms worse. When physically depleted patients will notice their mental faculties deteriorate, and they can become confused and forgetful.

NICE have recognised **Post Exertional Malaise (PEM),** also described as **Post Exertional Symptom Exacerbation (PESE),** as a cardinal feature of the condition. It is also recognised that patients experience deterioration after exposure to sensory stimulus – such as noise, movement, or light.

Even relatively trivial activities can trigger an exacerbation, with prolonged 'recovery' time. Typically ME patients will experience an exacerbation for days or even weeks if they exceed their limits.

Appearance On a personal note, I have observed that many young ME sufferers have a characteristic marked facial pallor with a translucent character. This is a diagnostic clue, but not confirmatory.

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AETIOLOGY

Although the aetiology of ME is not fully understood, scientific advances are revealing neurological, immunological, autonomic, and energy metabolism impairments. In my view the disease is best thought of as a multisystem disorder with an encephalopathic element, as this is the only way that the full array of symptoms can be adequately explained. For example, research has demonstrated consistent abnormalities of brain stem and cortical perfusion by scanning in adult ME patients (1). Unfortunately the relevant brain scans are not widely available.

While not primarily part of the aetiology of the disease, there has been good evidence that patients have decreased blood volume, and this can reduce cerebral perfusion. This has led to the use of repeated boluses of IV saline which produce temporary benefit in some patients. It might well be that colloid (synthetic or albumen) would work better as more longlasting, although I am unaware of anyone having tried this.

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NATURAL HISTORY OF ME

In a proportion of ME cases seen early, infection with an enterovirus or influenza can be documented. Some cases follow mononucleosis or hepatitis A. In the wake of the coronavirus pandemic, a growing number of patients are presenting with an indistinguishable clinical condition following SARS-CoV-2 infection: this is commonly referred to as 'long-Covid'. (Calling this 'Long Covid ME' has the advantage of protecting these patients from Graded Exercise regimes.) The remaining cases come on gradually and it may be difficult to date the onset of the disease.

This is an illness with a wide spectrum of severity and currently no effective treatment. A full spontaneous recovery is possible, often after several years. However this is not the norm. Most cases follow a prolonged course with fluctuation in the severity of symptoms and mini-remissions followed by relapses following further infections or other bodily stresses.

In general it seems that the overall prognosis is better for children and young people than it is in adults, particularly if the child has less severe symptoms. Severe cases can persist into adulthood with a very guarded long-term prognosis. Fortunately however, *some severe cases make complete recoveries.* Sadly, the reality is that at the extreme end of the spectrum of severity there are a small number of sad cases where the young person appears to have actually died from their ME.

Prognosis is undoubtedly improved if the patient receives – and follows – the best advice: to cut back on activity, with complete rest. This can also help reduce the severity of symptoms. This approach, which is endorsed by NICE, can be called PACING.

It replaces the previously popular approach of graded exercise or graded activity, which is now recognised to be not only ineffective but often positively harmful. This is recognised in the 2021 NICE Guideline, which states that patients with ME/CFS should not be offered "any programme that uses fixed incremental increases in physical activity or exercise, for example, graded exercise therapy" (NG206, recommendation 1.11.14).

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MANAGEMENT

Pacing is vital to achieve the best possible quality of life and to help avoid further deterioration. However it should be emphasised very clearly that there is no curative treatment available for ME. Patients quite accept this and it is often the doctors who find it difficult, and thereby fall into the trap of the 'Therapeutic Fallacy' whereby they can't accept the failure of their regimes. This can lead to them rejecting their patients with ME or, even worse, blaming the patient or family for the failure to improve.

I have been involved in >200 cases where children have been subject to Child Protection procedures and threatened with removal from their families in such circumstances. These cases could be seen as 'child abuse by professionals'. (2)

I personally start from a position of therapeutic nihilism and take it from there! Then one can accept that, as in any chronic illness, patients deserve lots of support. This comes in the form of the following:

Diagnostic Clarity

Simply making an official diagnosis is very important. In doing so the doctor shows that they believe in the genuineness of the condition and this **validation** is an important step in beginning to help and support the child and family. Explaining the implications of the diagnosis is not exactly 'good news', but it is best to be honest and the potential for bad news should not be glossed-over or minimised. The family need to be warned of the dangers of overdoing things in the early stages which can undoubtedly make things worse. Explain the guarded prognosis and the lack of curative treatment. Then offer **sympathy** and...

Support

Children with ME deserve just as much support and help as any child with a chronic illness. In my view, all but the very least severe cases merit long-term support from a consultant paediatrician, rather than simply being discharged to the care of the G.P. Practical help can include:

- writing to the school explaining the illness and how it manifests
- arranging Home Tuition for those too unwell to attend school
- supporting the needs for extra time to be allowed for exams and for rest periods during exams
- helping with Disability Living Allowance (DLA) claims and appeals
- putting in touch with ME support organisations
- for those attending university, making the case for granting residence on the ground floor and lodgings close to lecture halls

Protection

Children who have ME but lack a firm diagnosis of ME are at risk of being wrongly viewed as malingering or school phobic by their parents, teachers, peers and assorted professionals. The most important step in protecting them from this nightmare scenario is that they be officially diagnosed as having ME. It is important to get all members of the family ‘onside’ as it can be very upsetting for the child if, for example, a distant granny or non-custodial parent adopts a policy of disbelief.

In the challenging area of the very severe cases, I have found the young person needs protection from over-investigation and exposure to too many well-meaning professionals, as they can actually add to the stress rather than helping. If the paediatrician panics and refers to psychiatry, it is often the case that the child emerges labelled not as severe ME but as having ‘Pervasive Refusal Syndrome’, and subjected to inappropriate regimes.

It is this area that in my opinion justifies the use of the term **ME** rather than CFS because of its power and strong aura of organic illness. ‘Chronic Fatigue Syndrome’ is mealy-mouthed by comparison, and cuts no ice in the playground when a child returns to school after a gap of nine months! In the memorable words of one campaigner, Tanya Harrison of BRAME, *“the label Chronic Fatigue Syndrome is as unhelpful to ME sufferers as the term ‘Chronic Forgetfulness Syndrome’ would be to families and patients with Alzheimer’s Disease!”*

Another disadvantage is that most CFS definitions did not make PEM an essential feature, indeed some merely require ‘fatigue’. This may well have led to a clouding of the research narrative.

Symptomatic Treatment

There is quite a bit that doctors can do to help with symptoms such as pain and sleep problems. I have found drugs like Amitriptyline helpful for sleep reversal and pain, and Melatonin can also be very effective for sleep. Recently and surprisingly there has been evidence that Low Dose Naltrexone (LDN) can help with pain and energy levels (3).

A quite common comorbidity is Postural Orthostatic Tachycardia Syndrome (POTS), which can be beneficially treated with drugs like ivabradine.

My conviction is that ME is an organic illness, and that the role of psychological factors in the causation and course of this illness is around 0%. As with any unpleasant chronic illness there can be secondary psychological consequences. Naturally if psychological symptoms, such as depression, are present then these should be managed on their merits. If referral to psychiatry is being offered, make it clear that this isn’t in any way an act of disbelief in the genuineness of the condition. Similarly, avoid referral to ‘disbelieving’ psychiatrists in the first place as such consultations can be very upsetting for the young person and family, and counterproductive.

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THE CHALLENGE OF THE VERY SEVERE CASE

Paediatricians confronted with their first very severe case are naturally inclined to panic, leading to over-investigation, admission to hospital (which is usually very stressful, and counterproductive) and disbelief in the diagnosis leading to inappropriate psychiatric referral.

‘Take Home’ messages for the care of children and young people with severe or very ME are on the back page

Patients with very severe ME can be too weak to eat, swallow or speak. This is one reason why some cannot obtain adequate nutrition and hydration by mouth. Unfortunately they are at risk of being misdiagnosed as cases of eating disorder (4).

Tube feeding should be considered early rather than late as it can markedly reduce stress and energy consumption. Ideally the patient should be nursed at home wherever possible, and NG tube feeding can easily be carried out at home.

Patients with severe abdominal pain and digestive problems may be suffering from Mast Cell Activation Syndrome (MCAS), which may have contributed to a tragic string of recent fatalities. This condition can be amenable to treatment with oral cromoglycate (Nalcrom) and antihistamines.

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SUPPORT FROM ME CHARITIES

Naturally, the involvement of families with ME organisations both local and national is exceedingly important.

This is another justification for using the term ME, as all the support organisations use it, and there isn't a charity for 'Chronic Fatigue Syndrome'!

I have found in my area the support given by our local group absolutely invaluable and it has made my job of supporting children and their families that much easier. At national level, The Young ME Sufferer's (TYMES) Trust supports young patients and their families: I am a member of their professionals' referral panel (https://www.tymestrust.org).

POSSIBLE CURATIVE TREATMENT

The role of immunoglobulin deserves further study

Having stated that currently there is no curative treatment available, I believe that it is quite possible that the benefits of Immunoglobulin (IgG) have been underestimated.

Early work from Australia showed positive benefit from IgG. This included a randomised controlled trial (RCT) involving adolescent patients, one of the few treatment studies conducted on this age group.

I accordingly offered it to my 5 most severe cases and they all made full recoveries.

However, another trial showed improvement in the control group as well as the study group and a further, very small, trial showed no evidence of benefit. This was of course at a time when blood products were avoided as much as possible on account of CJD, strengthening reluctance to approve this therapy.

We have reviewed the evidence and in a 2021 paper argued for renewed consideration for IgG therapy (5). Two recent papers from Germany and Sweden have showed evidence of efficacy (6).

It would seem reasonable to consider a trial of this in individual very severe cases. While the RCTs entailed attendance at hospital for intravenous administration, it can be given at home via the intra-muscular or sub-cutaneous route.

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References

(1) **Brain scans indicate a reduced blood flow (hypoperfusion) that has not been demonstrated in any other medical condition:**

Costa D *et al.* (1995) *Brainstem perfusion is impaired in chronic fatigue syndrome*. QJM. 88, 11, 767-773. https://doi.org/10.1093/oxfordjournals.qjmed.a069004

Ichise M *et al.* (1992) *Assessment of regional cerebral perfusion by 99Tcm-HMPAO SPECT in chronic fatigue syndrome*. Nuclear Medicine Communications. 13, 10, 767-772. https://doi.org/10.1097/00006231-199213100-00011

Tirelli U *et al.* (1998) *Brain positron emission tomography (PET) in chronic fatigue syndrome: preliminary data*. American Journal of Medicine. 105, 3A, 54S-58S. https://doi.org/10.1016/S0002-9343(98)00179-X

(2) **Child abuse by professionals?** "Parents are accused of life-threatening neglect by letting their children rest in isolation. This attitude, however, ignores the international consensus definition of ME/CFS as a serous somatic disorder in which overexertion may have long-lasting or even permanent detrimental effects. To my knowledge, removing such patients from their parents has never been proven to be effective therapeutically. To the contrary, such non-evidence based practice has been shown to contribute much harm and should not be accepted."

Saugstad, OD. (2020) Editorial: *Myalgic Encephalomyelitis (ME) in the Young. Time to Repent*. Acta Paediatrica, vol. 109, no. 4, pp. 645–46. https://doi.org/10.1111/apa.15084

(3) **Positive reports of naltrexone:** "A positive treatment response to LDN was reported by 73.9% of the patients. Most patients experienced improved vigilance/alertness and improved physical and cognitive performance. Some patients reported less pain and fever…"

Polo, Olli, *et al. (2019) Low-Dose Naltrexone in the Treatment of Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS)*. Fatigue: Biomedicine, Health & Behavior, vol. 7, no. 4, pp. 207–17. https://doi.org/10.1080/21641846.2019.1692770

(4) **Severe gastro-intestinal problems and the professional response:** "The doctors failed to recognize the severity of the malnutrition or to provide appropriate nutritional support in a timely manner. Each case developed life-threatening problems as a result. In each case, the doctors resorted to making inappropriate psychological diagnoses without positive evidence of psychopathology."

Baxter, H.; Speight, N.; Weir, W. (2021) *Life-Threatening Malnutrition in Very Severe ME/CFS*. Healthcare 2021, 9, 459. https://doi:10.3390/healthcare9040459

(5) **Review of RCTs on immunoglobulin therapy:**

Brownlie H and Speight N (2021) *Back to the Future? Immunoglobulin Therapy for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome*. Healthcare, vol. 9, no. 11, Nov. 2021, p. 1546. https://doi.org/10.3390/healthcare9111546

(6) **Recent publications indicating efficacy of IgG:**

Scheibenbogen C *et al.* (2021) *Tolerability and Efficacy of s.c. IgG Self-Treatment in ME/CFS Patients with IgG/IgG Subclass Deficiency: A Proof-of-Concept Study*. Journal of Clinical Medicine, vol. 10, no. 11, May 2021, 2420. https://doi.org/10.3390/jcm10112420

Sjogren P *et al.* (2024) *Successful Subcutaneous Immunoglobulin Therapy in a Case Series of Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome*. Clinical Therapeutics, vol. 46, no. 7, July 2024, pp. 597–600. https://doi.org/10.1016/j.clinthera.2024.05.010

Children and young people with severe or very severe ME

≈≈≈ 'Take Home' Messages ≈≈≈

- Severe ME constitutes a major challenge for both patient and doctor.
- Mismanagement in the form of "activation regimes" can result in permanent harm or even death of the patient.
- The patient deserves the total commitment of one doctor, who is willing to visit at home on a regular basis.
- Referral to a psychiatrist who does not believe in ME/CFS can be harmful.
- The patient should be protected from sensory overload.
- The doctor should resist the temptation to over-investigate, or involve too many other professionals.
- Nursing at home is usually far preferable to admission to a busy general hospital.
- Tube feeding is indicated when the patient has problems with eating and drinking.
- Urinary catheterisation may be helpful in reducing the stress of having to micturate.
- Symptomatic treatment for pain and sleep problems is worthwhile.
- Full recovery is possible, but by no means guaranteed.
- There is a need to improve both undergraduate and postgraduate medical training in this area.
- There is a need to provide greater resources for the patient population affected.

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