

## Conversation Piece

Dr E.G. Dowsett is Honorary Consultant Microbiologist, Basildon and Thurrock Health Authority and is the President of the Myalgic Encephalomyelitis Society.

DR P.D. WELSBY: I, and indeed many general physicians, are often asked to see patients whose main complaint is 'tiredness all the time (TATT)'. From my previous experience also of general practice it seems that there is a wide continuous spectrum of debility ranging from a few days or weeks, but sometimes, distressingly, lasting for years. Such illnesses may or may not follow symptoms of an infection. Does the Myalgic Encephalomyelitis (ME) Society differentiate between post-viral debility, post-infectious (often an undefined infection) fatigue syndrome, chronic fatigue syndrome and ME? If so, how, and should it make any difference to medical management?

DR E.G. DOWSETT: One of the most striking features of ME is that the patient is *not* tired all the time! Extreme and sudden variability of energy levels both within and between episodes of illness differentiate this syndrome from other diseases associated with fatigue. One can only deplore the current fashion in the United States as well as the United Kingdom to redefine and rename a disability which has been clearly described in the literature for at least 100 years.<sup>1</sup> There is nothing to be said in favour of the American acronym CFIDS (chronic fatigue immune deficiency syndrome) with its connotation of a primary immune dysfunction. The term 'chronic fatigue syndrome' recently adopted in this country also is non-specific and non-descriptive because most of the definition is based on a vast number of exclusions (some of which, for example, endocrine disturbance, are actually found in ME). 'Post-viral fatigue syndrome', another British name, describes one essential feature (the association of the illness with viral infection) but gives the impression that the infection was antecedent rather than, as we now know, persistent. I prefer to use the more specific term 'myalgic encephalomyelitis' as it emphasizes the essential encephalitic component of the illness, the muscle pain, and the close clinical and epidemiological similarity to poliomyelitis.<sup>1</sup>

The medical management of ME differs greatly from that of other comparatively short-lived post-infectious debility, such as may follow influenza, in that the patient with ME has a 30% chance of cardiac and other systemic complications and must modify their lifestyle to a reduced capacity for as long as it takes the illness to stabilize. Early recognition and sensible advice to avoid mental or physical over-exertion, can do much to avert a prolonged chronic illness.

The essential clinical features of ME are not easily forgotten. They include:

1. Onset following a viral infection. This is more noticeable if, as commonly occurs, the individual has a good premorbid personality and work record (PDW). Surely ME will be just as prevalent in those with a bad personality or a bad work record – or are they immune? EGD. Point taken – this observation relates

- to a selection of patients with a clear date of onset for research purposes).
2. Generalized or localized fatigue made worse by exertion and not resolved by bed rest, with a prolonged recovery period out of all proportion to the energy expenditure. Such patients have reduced aerobic work capacity<sup>2</sup> and ultrastructural evidence of mitochondrial damage.<sup>3</sup>
3. Neurological symptoms indicative of hypothalamic disturbance (reversal of circadian rhythms, thermoregulatory, endocrine, neurotransmitter and water metabolism abnormalities, emotional lability), problems with balance and spatial orientation, rombergism, and sensory disturbances.
4. Associated syndromes. Cardiac (peri/myocarditis, orthostatic tachycardia with ectopic beats), endocrine (thyroiditis, pancreatitis, disturbance of carbohydrate metabolism), liver (mild hepatitis and bilirubinaemia), and secondary immunological disturbance (recurrent lymphadenopathy, leukopenia, circulating immune complexes).
5. Striking diurnal and cyclical variability of symptoms.
6. A prolonged relapsing course lasting years or decades.

PDW: I agree. Some doctors are inclined to view some stringent criteria for the diagnosis as gospel. The criteria advocated are often too stringent for 'general practitioner' use but are valuable in that all patients who fulfill the criteria almost certainly have the syndrome – which is necessary if one wants to ensure that one is studying a group of patients with complaints, some of whom might not have the syndrome. Obviously doctors have to exclude 'classical' organic illness but almost always there is no evidence of this and we, in the absence of a specific tests and specific treatment are left caring for the patient. It is my impression that most doctors are not perceived as being very successful in their caring, advising, and supportive role. Do you agree and how might the average doctor improve?

EGD: Obviously patients with ME are time consuming. The clinical examination and history taking must be painstaking and comprehensive. Most sufferers are forgetful, have poor concentration and fatigue rapidly. They cannot easily be fitted into a busy clinic. My own method is to adopt a scoring system and to persuade the patient either to bring a friend or relative with a good knowledge of the course of the illness or for them to write the symptoms out before attending. They are usually best managed at home, with social support, in the care of their GP, many of whom have become excellent diagnosticians after recognizing their first case of ME. Most patients speak highly of the care they have received from doctors who have had time to listen and who believe what they hear. The essentials of management are: (1) a clear explanation of the nature of the illness to the patient and their carers; (2) counselling so that their patient is enabled to accept the reality of the problems ahead and adjust to them accordingly; (3) assistance with mobility, education, and training; (4) support care and rehabilitation, as in any

other chronic illness, and early involvement of paramedical and other health care professionals.

PDW: I must say that dealing with such patients is stressful because one is never certain that one has excluded rare diseases or rare manifestations of common diseases. If I can make a 'classical' diagnosis then investigations and treatment, even if only palliative, are usually possible. Psychological or even psychiatric reactions to more severe or prolonged TATT illnesses are to be expected, yet why is there a profound reluctance of patients to accept that such factors might be operating as a secondary manifestation? Anxiety and depression can be alleviated although reactive depression may be unresponsive without removal of the underlying cause.

EGD: There is no evidence that patients with ME differ from the general population in respect of their psychiatric status.<sup>4</sup> They may, of course, suffer mental illnesses in a similar proportion to the general population and any such affected individuals should be treated appropriately. However the majority of ME patients are well motivated and do not have classical symptoms of depression. Hypothalamic disturbances in these patients may nevertheless give rise to mood swings and there is considerable interest and research into symptom modification using drugs aimed at hypothalamic dysfunction. It would seem unwise to use psychoactive drugs in an empirical fashion in ME patients unless there are definite indications. ME is a prolonged illness arising from chronic infection rather than a psychiatric disease and, as you say, any reactive depression will only improve with removal of the underlying cause.<sup>5</sup>

PDW: How long is the average patient with ME (I think we had better adopt this label for this conversation, especially as it is with the ME Society!) likely to be unwell?

EGD: The essential variability and relapsing nature of the illness does not provide any easy answer to this question. In general, there are 4 main patterns: (1) those who recover in 1–4 years (the average length of illness in young people is 4.5 years); (2) those whose illness fluctuates for a number of years; (3) those who eventually stabilize at an energy level which may or may not return to their former level; and (4) those who remain severely ill or go downhill from the start and become bedridden.<sup>5</sup>

PDW: There have been numerous claims for a whole host of dietary, fringe medicine, and drug cures. Is there any substantiated evidence that any dietary, fringe medicine, or drug treatment is uniformly effective?

EGD: No, there is no substantiated evidence for these remedies. Unfortunately there is no evidence for conventional medicine either, because we still lack the means to evaluate a controlled trial using *objective* proof of recovery. Empirical evidence is not satisfactory in an illness which may relapse outwith the observation period after some years of apparent good health. (For an interesting survey see reference 6.)

PDW: Why is it that ME patients are mostly young to middle-aged professional types? – hence the name 'Yuppie flu'?

EGD: The epidemiology of ME bears a striking resemblance to that of poliomyelitis in the pre-vaccination era; moreover there is historical evidence of immunological similarity between the two agents.<sup>7</sup> By 'virological analogy' this would imply that the interaction of hygiene (sanitation) and climate leaves the majority of British adults susceptible because they have not been naturally immunized by contact with the infectious agent in childhood. The viruses most closely associated with ME (enteroviruses, including polio, Cocksackie and ECHO-viruses) are spread mainly by asymptomatic children. Occupational exposure (teachers, health care workers, and parents) and the increasing susceptibility of the nervous system to infection from the age of puberty, means that ME is mainly an affliction of post-adolescent and middle-aged individuals in Western society. Cognitive disability is liable to prove more disabling in professional occupations, leading to prolonged sick leave and early retirement. Thus ME in the professional classes has received much media coverage and medical attention, leading to the undeserved pejorative term 'Yuppie flu.'

PDW: Some patients accept without reservation the advice to rest and allow themselves to become totally bedbound and dependent on others. Is there any way in which these unfortunate people can be encouraged to mobilize themselves? I often advocate rest but stress that, at almost any cost, patients should not retire from life.

EGD: A significant proportion of ME patients have a severe illness and go downhill from the start. Many suffer continuous pain (requiring referral to a pain clinic, since it may be thalamic in origin, or like post-herpetic neuralgia, may be caused by radiculitis), and some are extremely weak, anorectic and unable to swallow solid food. Their condition resembles other post-encephalitic or chronic encephalitis states and they require similar rehabilitation programmes. Unfortunately this need may not be recognized and the support care is often not available. However in at least one hospital patients with this form of ME are rehabilitated as if for head injuries. Many patients remain well motivated and courageous in spite of severe disability and make heroic efforts to mobilize themselves. We owe these patients respect, understanding, and first class care since there is no evidence that they are self-inflicted invalids.

PDW: There is of course the problem that anyone who rests totally for more than a few days will feel bad and get muscle aches and pains after resuming activity. Unconditional rest can precipitate a vicious circle if resumed activity leads to aches and pains which causes the patient to rest some more, and so on.

EGD: What is the evidence that rest for more than a few days makes patients feel bad and leads to myalgia on resuming activity? These complaints do not appear to affect rehabilitating patients obliged to rest for prolonged periods because of other medical conditions but who (like ME patients) can move freely in bed, walk to the toilet, and move to a couch in the daytime. Moreover the histology of muscle biopsies taken from ME patients shows mitochondrial damage<sup>3</sup> and type I/type II muscle fibre imbalance and *not* disuse atrophy. Muscle wasting (which occurs in about 3–5% of ME patients) is not

associated with rest, but *selectively* with use – for example, left infraspinatus muscle wasting in a harpsichord tuner who moves the left hand up the keyboard – and in areas such as the face which cannot be secondary to bed rest. The obvious reason for prolonged rest in some patients with ME are profound central fatigue, severe pain, and labyrinthine dysfunction. Whatever advice is

given, most patients with ME eventually learn that their illness will only stabilize when they exercise within their energy limits and avoid activity to the point of exhaustion.

PDW: Thank you.

#### References

1. Lyle, W.H. & Chamberlain, R.N. (eds) Epidemic neuromyasthenia 1934–1977: current approaches. *Postgrad Med J* 1978, **54**: 709–774.
2. Riley, M.S., O'Brien, C.J., McCluskey, D.R., Bell, N.P. & Nicholas, D.P. Aerobic work capacity in patients with chronic fatigue syndrome. *Br Med J* 1990; **301**: 953–956.
3. Gow, J.W., Behan, W.M.H. Amplification and identification of enteroviral sequences in the postviral fatigue syndrome. *Br Med Bull* 1991; **47**: 872–885.
4. Hickie, I., Lloyd, A., Wakefield, D. & Parker, G. The psychiatric status of patients with the chronic fatigue syndrome. *Br J Psych* 1990, **156**: 534–540.
5. Dowsett, E.G., Ramsay, A.M., McCartney, R.A. & Bell, E.J. Myalgic encephalomyelitis – a persistent enteroviral infection? *Postgrad Med J* 1990, **66**: 526–530.
6. Vallings, R. Myalgic encephalomyelitis – a consideration of treatment. *N Z Family Physician* 1989; **16**: 9–13.
7. Behan, P.O. & Behan, W.M.H. Postviral fatigue syndrome. *CRC Crit Rev Neurobiol* 1988; **4**: 157–178.