

Mental health problems in patients with myalgic encephalomyelitis and fibromyalgia syndrome

Byron Hyde

INTRODUCTION

Since 1934 at least 70 myalgic encephalomyelitis (ME)-type epidemics have occurred around the world.¹ Yet most physicians and the public remain unclear as to the cause and characteristics of ME. Many physicians debate the existence of ME as a valid medical entity. To put it kindly, many physicians simply find ME and patients with ME an unwanted bother. Since 1934, when the first well-documented ME epidemic ravaged the Los Angeles County Hospital,² ME as a diagnosis has refused to go away and the mental health aspects of ME and chronic fatigue syndrome (CFS) not only remain but also appear to increase. We require a better understanding of ME and CFS. Even with knowledge, treating the mental health problems of the patient with ME will remain a formidable task.

Since 1984, I have been asking the question, 'What is ME?' First I sought out the few original ME experts in various countries who had examined patients with ME and the ME epidemics since 1934. I examined patients and questioned physicians from the 1934 Los Angeles epidemic, the 1947–48 Iceland epidemic,³ and the various UK, New Zealand, Australian and Canadian epidemics, and I visited each of these epidemic sites. For the next 24 years, I have intensively investigated patients with ME and asked: 'What are the pathologies of the patient with ME that cause them to remain ill and unable to carry out the tasks that they were so good at before their illness onset?'

During the past 24 years, I have confined my practice to patients with ME and CFS. As much as possible, I have examined every organ and system of each of thousands of patients with ME, thanks to the totally free access that patients and physicians have to all tests and specialists in the Canadian health system.⁴ The following chapter represents a small amount of what I have discovered during the years that I have questioned ME experts, studied the considerable ME literature, and examined thousands of patients

with ME and CFS. What became obvious to me is that we cannot understand the patient with ME without examining the patient in great detail, along with his or her environment, social system and belief structure. We must also examine the limitations, usually imposed by government bureaucracy, that prevent physicians from adequately examining patients with ME.

THE WRITER'S PREJUDICE

Allow me to start by first acquainting you with my prejudice of what I believe constitutes a patient with ME, since it may interfere with any preconceived perceptions that you bring to this discussion. My prejudice is this: the patient with ME has been with us a very long time, undoubtedly many centuries, but it was only in the twentieth century that we had the technology and medical organization to distinguish ME as a specific illness category and a communication system (the Internet) that enabled these patients to find each other and group together, often much to the regret of the physicians and often with an inaccurate diagnosis not based upon scientific evidence.

A succinct definition of ME is this:

ME is an acute-onset, diffuse injury of the central nervous system (CNS) that in turn either provokes or is associated with organ, system and social pathologies that prevent the patient from effectively competing in their previous work and social culture.

Classically, ME occurs in epidemic and endemic periods, as in the 1934 Los Angeles, the 1947–48 Akureyri or the various UK epidemics. The onset of illness in both the historical and today's patients is often associated with an apparent infectious disease, immunization, and traumatic or toxic exposure in the immediate previous days or by repeated traumas in the prior weeks and months.

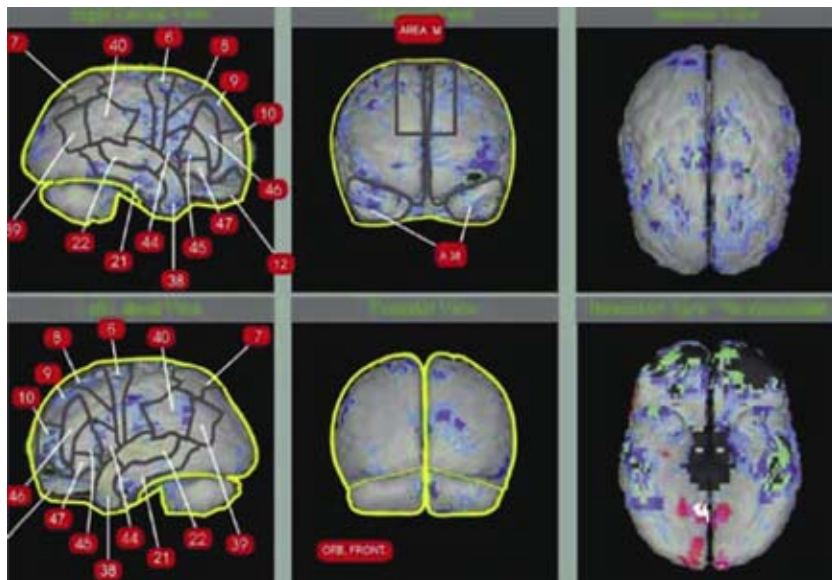


Figure 51.1 Brain single-photon-emission computed tomography (SPECT) of typical patient with myalgic encephalomyelitis (ME). This is a typical severe ME brain, as visualized by SPECT at illness onset, with Brodman areas indicated. Blue areas represent the significant typical hypoperfused areas of this dysfunctional brain. This schoolteacher fell ill following a severe influenza-like infectious episode 1 week after return to school. The patient went on to develop thyroid malignancy and *Clostridium difficile* infection several years later. Typical ME features: teacher, female, age 40 years at illness onset, post-infectious, no significant recovery during 15-year follow-up

The key terms in this definition are:

- acute-onset;
- diffuse CNS injury;
- complex organ, system and social pathologies.

Figure 51.1 shows a single-photon-emission computed tomography (SPECT) brain scan of a typical patient with ME.

In the clinical situation, both the physician and the patient are confronted with another problem. Which patient has ME? Which patient is misdiagnosed as having ME? Possibilities include the following:

- Chronic patients with ME and its associated organ, system and social pathologies
- Chronic patients with undiagnosed or missed single or cumulative major medical illness or pathology diagnosed as ME but suggesting low-grade or slowly progressive injury
- Patients with classical psychiatric disease that may or may not be complicated by organ or system pathology
- Acutely ill patients misdiagnosed as ME but with a potentially treatable progressive illness.

The first three patient categories above tend to have similar mental and social health issues and can be discussed as a group. By definition, the referring physician never diagnoses any of the missed major pathologies. If they did, then probably the patient would not be referred to as having ME or CFS. The big danger, the veritable mine in the minefield, is the last – the patient who, either diagnosed by a physician or self-diagnosed, has recent-onset ME. Too often have I seen fellow physicians who tell me they have ME, laugh and then say they do not require an examination, only to find that had they been examined properly an undiagnosed malignancy would have been discovered when it was still treatable. The greatest tragedy is to miss a diagnosis that

could have been treated, and perhaps cured, by the physician who had taken the patient's symptoms not as a diagnosis but as a medical mystery to be solved by scientific testing. This also represents my major criticism of the diagnosis of ME, either by the physician or by the patient. My criticism is not directed toward the psychiatrist but to the physicians who, for whatever reason, have failed to properly investigate and follow these reputed patients with ME before referring them to psychiatry.

THE PATIENT WITH ME AND HER MYTHOLOGIES

For the clinical psychiatrist and clinical medicine physician, it is the patient's complex mythologies, perhaps more than scientific understanding, that overwhelm both the patient and the physician. It is essential to understand these patient mythologies in order to help the patient with ME. Our patient is more than an injured body and brain: she is an integrated part of a complex belief and social structure with all of its values and prejudices.

If you were to be referred four real patients with ME, on average three would be girls or women and one would be a boy or a man. This 75 per cent percentage of females corresponds approximately to many autoimmune illnesses, such as multiple sclerosis and rheumatoid disease, but this of course does not validate ME as an autoimmune disease.

The child and adult sex distribution charts shown in Figures 51.2 and 51.3 were developed from an epidemiological study of approximately 2000 patients with ME or CFS investigated by the Nightingale Research Foundation during the epidemic period 1984–92. Note the significant divergence of females from males at puberty and the rapid drop in adult women new cases at menopause.

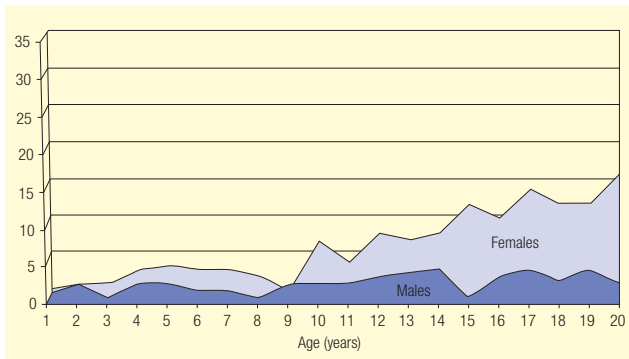


Figure 51.2 Sex and age of patients with myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) seen between 1984 and 1992 at the Nightingale Research Clinic: children and youths (age 0–21 years)

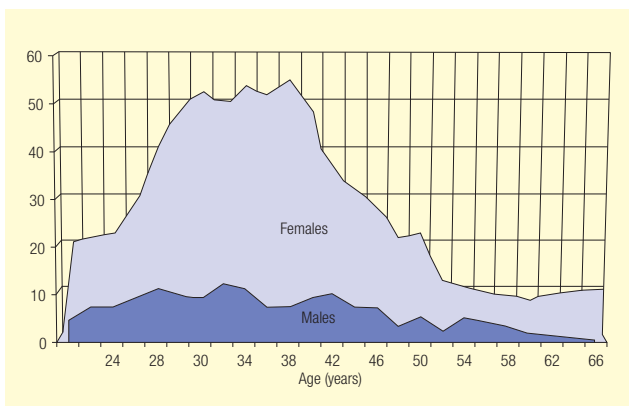


Figure 51.3 Sex and age of patients with myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) seen between 1984 and 1992 at the Nightingale Research Clinic: adults (age 22–70 years)

The patient before falling ill

From a mental health aspect, our patient with ME has a health history in addition to her present illness. Perhaps even more importantly, she has a vision of the future. The patient's past truly is prologue and the future is an existential necessity, both of which are capable of being destroyed. If you were to describe this young woman before the time when she fell ill, you would have acknowledged that she was a hard-working woman with many prior achievements and who contemplates realistic future goals. If she is in a long-term relationship, then in most cases she would have aspirations for her children, real or imagined, to do even better than herself. If our patient is a student, in most cases she will have all of the uncertainties, fears of youth, physical vigour and boundless energy, but also wonderful potential aspirations. Like Goethe's Faust, she has yet to learn that her existence is defined not by the goals but the very striving necessary to reach these goals.

Our patient before becoming ill will have already achieved a lot, including a higher education. Most often she

will be a teacher or healthcare worker with one or more degrees. You will note a strong school and healthcare bias to this illness, suggesting an increased exposure to infectious diseases and with long hours of exhausting work. To a lesser degree, the patient's occupation will mirror the local employment population bias, but the school and healthcare bias will be paramount.

The occupations of 2000 consecutive patients with ME were tabulated during the epidemic period of 1984–92 (Figure 51.4). These patients came from across Canada, the USA and, to a lesser extent, the UK. Consequently, the figures are not prejudiced by local employment. By percentage, the single largest occupation was among respiratory technologies, followed by healthcare workers, including physicians, nurses and technicians in residential institutions for disabled people, which may have an increased infectious rate.

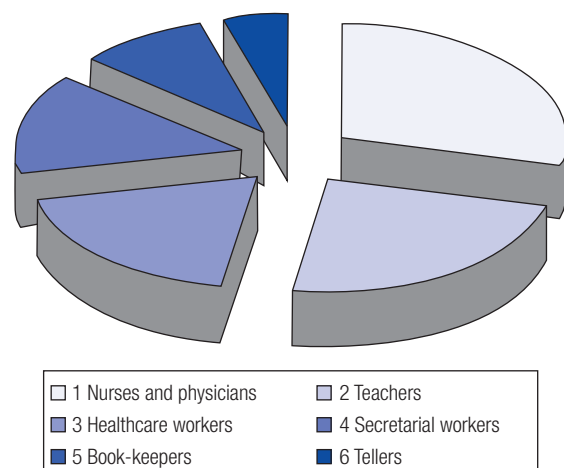


Figure 51.4 Occupation of patients with myalgic encephalomyelitis (ME) at illness onset

Often our patient will have been active in sports, with repeat associated minor and moderate physical traumas, often to the head and neck region. If you check her school record from kindergarten to the present, she will have missed a negligible amount of school. In most cases, before falling ill she will have had a history of excellent health, with no psychiatric associations. In my experience, except for those patients with a significant psychiatric family history, few of these patients with ME will be psychiatric patients. If you are an old physician like me, then our patient before falling ill will have been a person you would be proud to call your daughter. She will have an identity, courage, achievements and a belief structure with which you can associate. However, it is this belief structure as much as her illness that will provoke a significant part of

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what you perceive to be her illness. Thus, understanding her belief structure and her identity is important.

The patient's pre-illness identity and health belief structure

Our patient simply does not think about illness. If she is a parent, perhaps she has the natural concerns of any mother for her children, obtaining the right immunizations and paying occasional visits to the general practitioner (GP). She has never been significantly ill herself. Why think about illness? Visits to the doctor are for her pregnancies, routine Pap smear tests and breast examinations.

If you ask her about falling ill, she will dismiss the subject; illness is something short-term, a cold, perhaps off for a day or two and then back to school or work again. As a worker, she enjoys her job, the camaraderie, the striving; she loves her paycheque, even if it is too small – and it always is too small. She could be your daughter, your best friend's daughter or your granddaughter.

Life is simple for her. Should she fall ill and not recover sufficiently to return to work within a few days, she knows her GP will be able to diagnose and solve the problem with a pill or appropriate advice. Failing that, her GP will refer her to a colleague who will cure her and get her back to work.

If this first attempt fails, she knows that there will be a consultant or specialist out there who can appropriately diagnose, treat and cure her, but she never really gets to that concept, since the thought that her GP cannot treat and cure her simply never comes into her head.

Our patient has been working professionally or semi-pro-

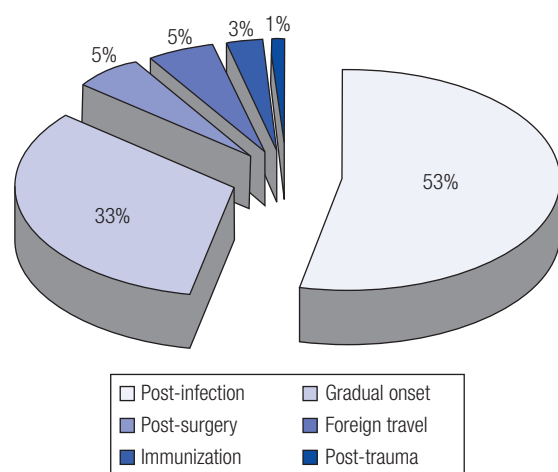


Figure 51.5 Triggers ascribed by the patient as a possible cause of their present illness in 2000 cases of myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS), 1984–1992. The gradual-onset patients tended to have no apparent associated triggers

fessionally for over 15 years without ever falling ill. Let us assume our patient is North American. She believes she has taken adequate steps to ensure access to good and prompt healthcare. She has both short- and long-term insurance coverage deducted from her paycheque. She will have a mortgage, but she may not have taken out mortgage insurance, skimping on this to pay for her child's piano lessons. In any case, if she does fall ill for a few weeks or months, say from a compound fracture in a skiing accident in the French Alps, then her disability insurance will cover her expenses. No, she has never looked at her insurance policy. Why should she?

In the more than 2000 or 3000 patients with ME and CFS who have consulted me during the past 25 years in Canada, the UK and the USA, before their illness the majority had a long history of health, free of any serious medical or psychiatric illness; very few ever imagined themselves becoming ill with a chronic illness. Illness triggers are not always reliable as a cause of illness in all cases, but the data in Figure 51.5, taken from a large survey of almost 2000 patients, are perhaps reliable as rough casual indicators.

The disintegration of the patient's belief and identity structures

Our patient's carefully constructed mythology of enduring health until old age, and her perceptions of the infallible medical world, are about to be destroyed.

What will now confront our previous worker bee and future patient amounts not only to a total destruction of her most important belief structures but also to the ultimate loss of her identity, an identity carefully constructed since youth.

The young woman falls ill. Her illness usually has an acute onset, but it is not short-term. From then on, nothing works, nothing unfolds in the manner she might have perceived it before the onset of this strange illness.

She does not become better in 2–3 days. In almost all cases, her doctor does not appreciate that he or she is dealing with the onset of a chronic illness. Since most acute illnesses tend to resolve on their own, her GP tells her that she will be fine in another week. That does not happen: her illness persists. Then or at the next appointment, her GP may prescribe a medication or treatment and may send her for a few tests, usually a complete blood count and a urinalysis and not much else. The tests tell her GP nothing because he or she does not know what tests to order; nor does the GP know at this point what he or she is dealing with. Sooner or later her GP will refer her to a consultant.

'No findings of note,' the reply comes back. 'Perhaps your patient is depressed?'

If her GP has not made the diagnosis by now, he or she soon will. It is likely to be anxiety neurosis, depression, work avoidance or family dispute – all diagnoses that are safe to make, all of which have no proof. Often notations in the history are not told to the patient; these notations, when

sent on to the next doctor or other agencies, may undermine the patient's later chance for insurance benefits or state incapacity or disability allowances. The doctor is thus protected, but not necessarily the patient. Our patient may even be given an antidepressant that, over time, succeeds only in significantly increasing her weight. Usually the patient is given a psychiatric diagnosis by the GP and referred to a psychiatrist, although there has been no previous psychiatric history. At times she may believe her GP that she is depressed; more often she does not. Even if the doctor diagnoses ME, he or she is unable to treat ME adequately. There simply is no magic pill and no remedy, and there is very little valid knowledge about the significance of the diagnosis. The psychiatrist immediately is at a disadvantage: he or she believes that physical disease has been ruled out. Yet physical disease has not been ruled out, and in most cases it has not even been seriously investigated. Our patient is now labelled 'ME or CFS', but often the doctor thinks anxiety neurosis, depression or conversion disorder. If the doctor thinks CFS, then this is no more than a poorly defined label; if he or she thinks ME, then this may be the least properly investigated epidemic and endemic illness in existence. In the UK, very few of these patients so diagnosed have ever been subjected to any significant scientific investigation; many have not even had a serious physical examination.

Weeks and even months go by. No medication and no treatment works. Nothing works and the illness persists.

Within 2 months, her disability insurance raises its head. Since there is no documented evidence for any significant illness, her insurer does not bother paying. Sweet soul that she is, she honestly believes that if the insurance company only knew how ill she were, then it would send her a disability cheque. The insurance company has a good cop who pretends to be the patient's friend, talks her into going back to work or tells her the company is just waiting for a few more results to be sent in. She tries to go back to work and falls flat on her face. Before long, a year has gone by and in many cases the insurance company still has not honoured the disability pension. Some insurance companies actually guide the patient along until it is outside the time limits for her to make a qualified application for benefits. By now, much if not all of her savings have been dissipated. All ballast, including her child's music lessons and the piano, have gone. Rapidly she is stripped to the economic bone. If she has not been frantic up to now, she soon will be.

The search

Our patient, worker bee that she is, after months and possibly a year or two, having failed to find a helpful doctor and failed to have been awarded her disability pension, searches the Internet for an expert who will treat her. Her GP and often her family and friends have given up on her. Yet she cannot believe that there is not someone out there who can diagnose and treat her and get her back to work, give her

back her family, paycheque and friends, and restore her identity. She amasses reams of garbled information, which is often misinformation – but she does not believe this. She is going to educate her doctor about the 'true facts' about ME. However, on the Internet, she also encounters mixed with the fact some of the most incredible hogwash imaginable; she will meet some of the slickest charlatans in the business, the penny-and-pound thieves who sell her miraculous alternative medications that do not work and sometimes kill. Before long, our disabled patient is paying out, in effect gambling, incredible sums of her much-needed money in the vain hope that these miracle cures will soon make her better and get her back to work. They do not work.

Some of the more brilliant charlatans, the highwaymen of the twenty-first century, will guarantee to restore her health: 'Our treatment has saved thousands of people, but this treatment is expensive, very expensive, but isn't your health worth it?' She bites! If she or her family are desperate enough, they will sell their house, invest their life's income in a desperate gamble not to lose all. They lose all! Sometimes she will lose her family; but worse, she will lose her carefully crafted identity as a proud member of her community, a successful worker and a student of life. She loses all that she was and intended to be. She cannot even be a good mother. She thinks about the piano lessons that have stopped and the piano that has moved out, and she feels that she is now failing as a parent. Nothing works.

Several times she tries to go back to work but simply cannot endure. Since she has no adequate psychiatric or physical diagnosis, her long-term insurance policy has either stopped after a short while or in many cases has never begun. The insurance companies know these patients well. They know their client has no funds, no physical energy and no resources to fight back. Our patient's partner may have left her; he can no longer take the expense or handle chronic illness, the lack of sex, his wife's inability to even go out for a show. Alone, or with her children, she may return to live with her ageing parents. Without supportive parents, she may fall into a life of welfare benefits and despair, barely eking out an existence. She may kill herself. Only if she is one of the wealthy few, one with funds that are not wasted, or who succeeds in obtaining her disability pension is our patient able to survive with any integrity. Many patients become bitter, writing diatribes, attacking authorities, doctors included. Many doctors simply lump them all into one more group of nutters.

She will have been referred to you, a psychiatrist. You are kind to her. You speak in a soothing manner. Having lost everything, at last she has found a friendly ear, someone who will believe her. She cries – a sure sign of depression – and out comes the prescription pad for the first of an endless series of antidepressive medications that succeed only in making this normal-looking athletic woman into a fat blimp and still unable to return to work. If our patient resists this treatment, she is written off as 'not complying'.

DOCTORS: THEIR FEAR OF EMBARRASSMENT AND THE ECONOMIC REALITY

Let me introduce you to a few of the doctors that this woman has consulted. Like our patient, these doctors have their own history and mythologies.

Most doctors were some of the top students in their primary and secondary school systems. Then they were enrolled in medicine, where they met hundreds of other medical students with a history of being at the top of their class. Only a few of the hundreds of these medical students can ever expect to be at the top. Only a handful would be considered to be the most brilliant and have honours bestowed upon them. No one doubts that the top students would be truly brilliant. But, depending upon the school and the teacher, their brilliance may in large part be the ability to give back a wide range of accepted fact in a clear, concise, organized manner. It is a curious thing that many of the very top students do not continue in clinical medicine. They are not always interested in people as much as they are in excellence. The majority of the other graduating doctors in their class fall into other groups, and those who have not lost their curiosity may become some of the very best clinical physicians and researchers. Yet others who have always been first, the best in their class, have been needlessly embarrassed at not being one of the exalted top few. For many such students of medicine, this may be the end of independent thinking, of exploring, of challenging the accepted wisdom. It is precisely this need not to be embarrassed further that caused doctors for centuries not to discover circulation or the concept of infectious disease and almost every modern aspect of medicine. For centuries, they survived by embracing the accepted wisdom.

There is another problem concerning the referring GPs who will refer the patient with ME to you. During the past 40 years, except for a few subspecialties, most doctors' real taxable incomes in North America, the UK and Western Europe have fallen from one of the highest in the community to that of a modest middle-income person. You may be earning less than your patient with ME was earning before she became too ill to work. The doctor starts in practice with debts. Without help from their parents, in most cases there is no way that doctors in North America can afford to buy the house that any doctor purchased 40 years ago or even 20 years ago. The medical magazines talk about making your practice more efficient, which essentially means seeing more patients for less and less time. Essentially, that means getting the patient out of the clinic by giving them a pill, sometimes any pill. They and you pretend this is not so, but you too have a mortgage and your partner expects you to buy that magical piano, pay for your child's piano lessons and the family trips to ski in France this winter, or simply take that cruise advertised in the doctors' magazines. Unless you take a government,

pharmaceutical industry or insurance company job as a doctor, or you succeed in getting one of the senior positions in the hospital on a salary, unless you work a 60-h week or see patients outside the National Health Service (NHS), not only will your income be modest but also you will be judging yourself against an unrealistic measuring stick of those doctors who have come before you and a few of your colleagues who appear to be wealthy. You simply do not need a troublesome, complicated patient with ME who will take up your valuable time.

I am still talking here primarily about the non-psychiatrist physician. Money is status. Time is money, and few can take the time to explore the incredible significance of the relatively young chronic patient with diffuse brain injury. These patients with ME simply take too much time. Consequence? The primary care doctor simply sends the patient with ME to the psychiatrist, who they believe has all the time in the world. The psychiatrist in turn will assume that, as in all reputed psychiatric patients, the primary care doctor and the consultant have adequately investigated the referred patient who now sits in front of them. Yet you, as a doctor, should know better – and many do. The system in the UK prevents most primary care doctors from even ordering a full technological evaluation of their patient. The system in the UK, North America and much of Europe does not give the doctor time or money to explore this fascinating patient. Worse, there are no specialty clinics working inside the NHS that have the time, authority or financing to properly investigate these patients with ME for physical cause of disease. This total chronic failure to systematically examine the patient with ME has not been helpful, either to the patient with ME or to the psychiatrist.

The relatively young, chronically physically ill public in the UK tend to be very critical of the psychiatrist, and often needlessly so. Yet, as a psychiatrist, you have both a disadvantage and an advantage over the regular non-psychiatrist. The disadvantage is that your income may be one of the lowest in the medical community. The advantage is that your expenses are less and you alone among your colleagues will be able to listen to your patient for a considerable time. Perhaps you will be the first doctor who has the time to listen to her and who can get to the physical route of her anxiety, even if you cannot improve her material life. It is here where your difficulty becomes even more complicated.

Like many of your medical and psychiatrist colleagues, you will not want this patient. She simply takes up too much time in the clinic, and you wish to see her depart so that you may get on to a treatable patient. Many of your own psychiatrist colleagues will believe that any patient with ME is simply expressing some form of hysterical behaviour, is a whiner, is someone who does not want to work, or, worse, is boringly uninteresting. The patient will believe she knows much more about ME than you do; perhaps she does, but that is irritating to you and often her information is as highly inaccurate as yours has been. We

are now looking at a major treatment impasse, including hostility, which may be mutual, and poorly organized information on both sides.

There is one final aspect to these patients with ME. Few patients realize the two-way nature of medicine, the great joy of being a doctor, of making a clear diagnosis of the patient and getting that ill patient either back to health or at least to a position where they can manage. Yet this patient with ME is not some fascinating patient with bipolar disorder from the Bank of England who has just ripped through a few billion pounds of your country's money. She is not a schizophrenic poet of immense talent and immense self-destructive powers. This is not a case where there is a good chance you can bring banker or poet back to reality. It is so easy to tell yourself that this is one more case of ME hysteria.

How can you, the psychiatrist or for that matter any doctor, help this young woman?

If you catch the patient in time, you can attempt to help this unbelieving patient to stop wasting her valuable and decreasing funds on bogus care and treatments, usually from non-doctors. If you believe that the patient is significantly disabled, and in my experience few patients in this category ever lie and most are more disabled than even they realize, then you can help her obtain appropriate state benefits or her entitlement to disability insurance. More than any other assistance you can provide, this may help her save part of her identity and perhaps her life, and she will bless you for it forever. This may take work, and it would be good to have a psychiatrist colleague or ombudsman whose work is limited to handling these matters to which you can refer this patient. It takes both significant time and skill in assisting these patients with the insurance industry and benefits systems.

It is not only the uninformed doctor who represents a problem but also the reputedly informed patient. Both doctors and patients have bought into the nineteenth-century Oslerian principle that the best way to treat and possibly cure a patient is to diagnose the illness as to the cause, treat the cause and, with knowledge and luck, cure the patient. The problem is the phrase 'the cause', since many of these patients have multiple causes giving rise to their disability. This unicausal theory of medical pathology worked for pulmonary tuberculosis, for syphilis, so why not ME? Well, what if there is not a single cause of the illness? What if the patient with ME is disabled due to multiple cumulative pathologies?

MULTIPLE PATHOLOGY PATIENTS

My clinic is in the process of an in-depth study of the last 53 consecutive patients referred to us with a diagnosis of ME or CFS. In this group:

- 100 per cent had missed measurable brain dysfunction;

- 98 per cent had measurable significant sleep dysfunctions that included (i) lack of type 3 and 4 sleep, (ii) abnormal, absent or significantly delayed rapid eye movement (REM), (iii) central and peripheral apnoea, (iv) restless legs syndrome and (v) oxygen saturation that fell below 88 per cent (interestingly, oxygen saturation below 88% caused loss of consciousness in an aircraft pilot);
- 74 per cent had measurable thyroid dysfunction;
- 47 per cent had measurable significant arthritic, rheumatoid changes or other indicators that were previously diagnosed as fibromyalgia;
- 47 per cent had other missed major disease, including cardiac disease, malignant disease, vascular injuries and autonomic nervous system dysfunction;
- at least 16 per cent had typical psychiatric illness but, in addition, missed physical disease.

The problem here is not the multiple pathologies but the fact that the primary or consulting doctors missed these multiple diagnoses.

We subdivided the 53 patients in this study under occupations. This is what we found:

- Nineteen patients (37%) were school-associated professors, teachers or students.
- Nine patients (17%) were civil servants, the majority with young children in school.
- Five patients (10%) were healthcare workers.

This study of a group of 53 patients with ME/CFS was biased due to the fact that in Ottawa, Canada, a large percentage of the inhabitants are government workers. In an earlier study that looked at 2000 patients from across Canada and the USA, school and healthcare workers represented over 70 per cent of the 2000 patients. This suggested that ME was usually associated with a high exposure to infections.

As noted in the group of 53 patients, the single largest group was 19 (37%) of the total. These were students and teaching staff at primary, secondary and university educational institutions. For brevity, I will confine this discussion regarding pathological findings to these 19 patients referred to me as patients with ME who were teachers and students. This dominant group also contained the largest number of youths and children.

Collectively, these 19 school-associated patients had been seen by over 200 doctors. All had missed the following pathologies, which were found by extensive history, physical and technological examinations:

Dysautonomia and postural orthostatic tachycardia

Check your patient's arterial blood pressure, pulse pressure and heart rate when they are lying, sitting and standing. Have your patient stand without moving and check their

blood pressure every minute for 10–15 min, stopping if their pressure drops precipitously or their heart rate accelerates above 120 bpm. If you find the blood pressure falling or the pulse pressure narrowing significantly, immediately stop the test and ask the patient to sit down. Make one of your first patient visits a 2- to 3-h visit in order to obtain a full life history. Note how many times the patient has to go to the toilet during this visit, suggesting possible pituitary or other endocrine disease. Do not allow the patient to have a water bottle with her during this time.

Measurable brain disease in patients with ME

A surprising 100 per cent of the 19 teachers and students had significant brain changes or anomalies by one or all of technical examination, measurement or history. If you can, order or have your medical colleagues order a brain SPECT, a magnetic resonance imaging (MRI) scan with contrast of the brain that includes pituitary, cerebellar tonsils and cervical spine area.

As mentioned earlier, the following pathologies were missed by over 200 examining doctors, who possibly did not believe they were dealing with significant physical disease and so did not do an extensive examination of these patients. We found the following:

- A patient with tertiary CNS syphilis and who was also positive for hepatitis B diagnosed as having simple major depression
- Leucoencephalopathy with ventricular hypertrophy in a youth
- One adult with significantly abnormal electroencephalograms (EEGs)
- One youth with missed nocturnal seizures and seizure-associated episodic complete heart block, causing syncope, significant hypoglycaemia and obstructive chronic tonsillitis that occluded his pharynx when sleeping on his back
- A youth with Chiari syndrome with ventriculomegaly
- An older patient with significant generalized brain atrophy and ventricular hypertrophy
- A patient who had been in the area of the Chernobyl disaster as a 1-year-old child and who had a subarachnoid cyst that had displaced two-thirds of the left hemisphere, including the entire left frontal lobe, the entire left temporal lobe and the anterior part of the left parietal lobe, but who had no observed neurological examination abnormalities either on neuromuscular examination or in gross intelligence. He simply had overwhelming exhaustion. He had graduated with an master's degree
- A patient with complete atresia of the middle cerebral artery
- A patient with multiple CNS vascular changes.

In addition to these findings, many patients had major SPECT brain changes in both hemispheres, the midbrain and the brainstem.

The average age of these 19 students and teachers was 33 years.

Two of the 19 patients had incapacitating autonomic nervous system dysfunction. One, a master's student who fell ill immediately following recombinant hepatitis B immunization and is now house-confined, has a highly positive tilt table test and is unable to maintain her blood pressure at a physiologically normal level while standing or on movement.

The rewards in properly investigating this group of patients are significant. Although we did not find any patients with multiple sclerosis (MS) in this group of 19, we did pick up a missed case of MS in the total group of 53 consecutive patients and a surprising number of single large (diameter ≤ 2 cm) CNS demyelinating lesions that do not qualify as diagnostic of MS. Each of the patients with non-MS single-lesion demyelination was associated with markedly abnormal SPECT brain scans. Also in the group of 53 consecutive patients, but not in the school-associated group, we found a missed significant brain aneurysm in addition to numerous other organ pathologies in the same patient. The aneurysm has since been repaired. Another patient had a right lenticular haemorrhage, which the neurologist then dismissed as minor; on SPECT we were able to demonstrate a 3- to 4-cm halo of abnormal activity around the lenticular lesion consisting of highly significantly hypoperfused brain tissue. In addition, we observed a decrease in perfusion in the entire right lobe of this patient, but with a normal left hemisphere perfusion. Clearly some localized non-motor cerebral accidents may provoke profound generalized CNS changes.

Are these all patients with ME? No, of course not; but in real terms, it does not matter. These individuals were all diagnosed as having ME or CFS by otherwise competent doctors who dismissed the patient when they came with a diagnosis of ME. These will be the same people who are referred to you as patients with ME by GPs and internists who simply think these patients complaining of acute or gradual-onset fatigue and cognitive dysfunction have ME or CFS and either have no idea how to investigate them or simply are unwilling to take the time to do so.

Thyroid disease in patients with ME

For some reason, the centuries-old medical knowledge of the physiological association of thyroid disease and intellectual, emotional, psychiatric, cardiac and other endocrine pathology seems to have escaped the 7 min-per-patient visits of many primary care and specialist doctors. Most non-psychiatrist doctors limit their examination of the thyroid to a cursory palpation of the gland for nodules and perhaps order thyroid-stimulating hormone (TSH) and free thyroxine (T4) tests. In most cases these doctors will not find disease. It is essential to request a thyroid ultrasound on all patients with ME. In addition, the doctor must ask the ultrasound technician to give the measurement of each thy-

roid lobe; if you do not, the technician or the doctor reading the ultrasound result will often just say 'normal' if there are no nodules or the gland is homogeneous. Why the measurements? Simple: the Mayo Clinic normal thyroid sizes are 13–21 cm³ for females and 15–23 cm³ for males. They arrive at these figures by multiplying together the three dimensions of each lobe and adding the left and right lobe measurements as though the thyroid were a regular rectangle. This is not the actual size of the thyroid. If you have access only to an old ultrasound device, then the radiologist may give you these crude rectangular volumes. It is necessary to multiply these volumes by a factor of 0.51. This will give you the approximate normal thyroid volumes of two irregular solid spheres. The real volumes are then half the Mayo suggested volumes, or 6.–10.5 cm³ for females and 7.5–11.5 cm³ for males. It is important to know this, since modern ultrasound machines give this calculation in terms of the 6.5–10.5 cm³ female thyroid volume scales. These are not gold standards, but if you bring in a thyroid at less than 4 cm³ or over 15 cm³ you know you are dealing with an atrophic or hypertrophic thyroid, respectively, with possible intellectual, emotional and psychiatric consequences. Sometimes, simply by appropriately treating these patients with T4 or tri-iodothyronine (T3), you can cure their fatigue and cognitive dysfunctions. (Note: patients on previously prescribed or over-the-counter thyroid medications may have a hypotrophic thyroid.)

Nor can you count simply on the usual TSH, free T4 (FT4) and free T3 (FT3) thyroid tests that are stated as normal or slightly abnormal. If the basic injury to the thyroid is vascular, as I believe it to be in most ME brains, then often the parathyroid hormone (PTH) and the ionized calcium will become abnormal before the usual thyroid tests. I do all of these tests, including thyroglobulin, thyroglobulin antibodies and microsomal antibodies, as well as an ultrasound, on each and every patient with ME that I see. In the group of 19 teachers and students in our group of 53 referred patients with ME, we found 14 patients (74%) with abnormal thyroid activity. I have also found several patients with new-onset ME with normal initial thyroid chemistry but with a significantly shrinking thyroid when the ultrasound was repeated in 1–2 years, which may suggest a vascular problem.

In the last 100 patients with ME/CFS, we also have found missed thyroid malignancies in 6 per cent. Some doctors discount this figure, since thyroid malignancies are considered to be common and not particularly dangerous, but that is not true for a young population. In one of the group of 53 patients, we discovered a thyroid malignancy that had already disseminated.

There is one more thing you must know before we leave the thyroid. T4 does very little on its own: T4 must first be discharged into the bloodstream and then transported to the liver and kidneys, where one of the iodines is removed to make T3. If there is pathology in this conversion, then an isomer called reverse T3 is made. In simple terms, the

importance of this is paramount. T3 is one of the keys that turn on each body cell. If your patient is producing too much reverse T3, then this reverse T3 fits into the cell's energy receptor and breaks off, and the cell energy cycle cannot function normally. All the T4 in the world will not help this patient: she requires T3. Is it enough to ask for a reverse T3 level? No! Often the laboratory will give you a reverse T3 level in the normal or high normal range. You need also to order an FT3 at the same time and then divide the reverse T3 level by the normal T3 level; if the result reaches 10 per cent or more, your patient probably requires exogenous T3. But be careful: these patients with ME tend to be very medication-sensitive, so you should start at 5 µg daily, increasing every 2–4 weeks until you reach 25 µg and then stay at that dosage for some months before considering raising it to a normal dosage or subnormal dosage. If the patient has a heart condition as well, take advice from a cardiologist on the safety of giving T3 to this patient. All of these patients want to get back to normal in 5 min, but this is dangerous if part of the problem is thyroid dysfunction. Starting T3 at too high a dosage or increasing the dosage too rapidly may provoke seriously irregular heart rates, irregular cardiac rhythm and rapidly altering blood pressures. It may take up to a year or longer to slowly restore the patient with ME to normal thyroid levels.

Sleep dysfunction

All patients with ME should have at least one sleep study and some sleep studies with film monitoring to observe the presence of nocturnal seizures missed in daytime EEGs. In our group of 53 patients, we found only one patient with a normal sleep study; her dysautonomia was so severe that she was in a state of vascular collapse. Some authorities state that the abnormal sleep study can be blamed on the way the study is done, or the hospital environment in which these tests are performed, but generally these patients have non-restorative sleep. In our studies, 70 per cent of the 53 patients had no stage 3 or stage 4 sleep. This is the sleep phase where short-term memory is laid down. In addition, 77 per cent had grossly insufficient REM and very long REM latency. Among other functions that occur during REM is the burning into the neuron system of short-term memory: it is no wonder, then, that these patients describe short-term memory loss.

Interestingly, if the oxygen saturation falls below 92 per cent, commercial pilots become both colour- and night-blind and have difficulty landing their planes during the night. If the oxygen saturation in the cockpit falls below 88 per cent, the pilot has a good chance of losing consciousness and crashing the plane. Accordingly, oxygen saturation is monitored carefully in the cockpit, although less so in the passenger compartment. In our study of 53 patients, the oxygen saturation in 25 patients (53%) fell below 92 per cent during the sleep study; the oxygen saturation in 17 patients (30%) fell to 88 per cent or below. In other words,

they were not sleeping; they were unconscious. The oxygen levels at least are potentially correctable pathologies.

Respiratory dysfunction

In our group of 19 students and teachers, ten patients (53%) had some measurable respiratory dysfunction. We did not count a history of asthma in this group, although in many patients there was an obvious overlap. Had we included a history of asthma, it is possible that even more patients would have had measurable respiratory dysfunction.

Missed miscellaneous disease

In our group, 47 per cent of patients had major missed illness, including the following:

- A case of tertiary syphilis and hepatitis B
- Four patients with significant heart disease
- A patient with respiratory dysfunction with significant pulmonary valve disease
- One juvenile and two type II cases of missed diabetes
- One patient with Ehlers–Danlos syndrome
- Numerous rheumatoid and significant spinal anomalies.

Although two patients had significant incapacitating autonomic nervous system dysfunction, several had lesser degrees of measurable dysfunction.

One patient in the group of 53 patients was a young lawyer and Olympic runner. He was referred to me as a patient with ME due to extreme fatigue and had Marfan-like anatomical changes. He had a missed hyperelastic distended thoracic aorta picked up on echocardiogram. In addition, he had lumbar dural ectasia on computed tomography (CT) scanning (seen in 65–92% of patients with Marfan's syndrome). At least seven doctors had each missed this diagnosis. The patient was denied any family history of Marfan's syndrome until he was asked to enquire of his remote cousins. Three of his second cousins had a family history of ascending aorta surgical replacement in their twenties. The cause of his thoracic aorta pathology was complicated by the fact that he had been infected with brucellosis while training in South Africa. Brucellosis can also cause aortic aneurysm. A detailed extended family history is essential in investigating ME-type patients.

Psychiatric disease

Patients with ME like to believe that there is no psychiatric disease associated with ME. Some psychiatrists and primary care and specialist doctors like to believe that 100 per cent of patients with ME have psychiatric disease. What did we find? Many of these patients with ME had been referred to psychiatrists before our examination of them; six patients (32%) were diagnosed with primary psychiatric disease. After we had finished our investigation, we found only three patients (16%) with treatable psychiatric disease. There are several reasons for this discrepancy. We believe

that some psychiatrists, to assist a destitute patient with ME, may give a psychiatric diagnosis simply to assist the patient in obtaining their disability pension.

Let me give you a brief review of some of these psychiatric patients.

The patient with tertiary syphilis was first diagnosed with unipolar or major depressive disease. This patient also had hepatitis B.

Another patient had major childhood abuse, during which time she was placed in a reformatory and also various psychiatric hospitals in Switzerland by the woman who had adopted her as an infant. This incarceration first occurred when the patient reached puberty and may have been due to the mother's sexual jealousy of having another female sharing her ambassador husband's innocent affections. On her own resources, my patient obtained her master's degree, became a secondary school teacher, and is fluent in English, French, German, Italian, Spanish and Latin. There was obvious trauma. Today, aged 53 years, she is exhausted, perhaps simply worn out, and she certainly has anxiety and depression.

A third teacher, also adopted, initially diagnosed as having depression, has serious food addiction, which in itself has caused multiple medical problems. He certainly has no overt psychiatric illness, but he does have brain dysfunction and memory disorder. He also had missed generalized vascular disease, missed diabetes and missed myocardial infarct and is one of the two patients in the school group with generalized atrophic brain syndrome.

The husband of another patient, also a teacher, committed suicide; the patient has made two attempts on her own life and was reasonably diagnosed as having unipolar or major depressive disease.

Two other patients were diagnosed as having unipolar depression. Both had seronegative rheumatoid arthritis and both had measurable significant heart disease.

Each of these six patients also had other major physical pathology. How many of the six were truly classical psychiatric diseases? Probably three, or four if you count the teacher with brain atrophy and cognitive dysfunction. What is most incredible is the truly remarkable resilience of some of these patients despite their multiple organ and system disease.

Do these 53 consecutive chronically ill patients have ME? Is that important? Doctors who believed that the patients had ME or CFS referred all these patients to me. The same patients will be referred to you with the same bewildering array of pathologies. Can you afford to dismiss them as psychiatric patients if they have not been properly investigated first? Since all of the definitions of CFS and to a lesser extent those of ME are based upon symptoms common to a multitude of serious pathophysiological illnesses, under the present understanding of ME and CFS, doctors, whether primary care, consultant or psychiatrists, cannot simply dismiss these patients without first documenting an extensive investigation of the individual

patient. A thorough investigation of the chronically ill younger patient is fundamental to good medicine.

DEFINITIONS OF ME AND CFS

You may remember the lines of Mathew Arnold's poem 'Dover Beach'. ME and CFS definitions are a bit like that.

And we are here as on a darkling plain

Swept with confused alarms of struggle and flight

Where ignorant armies clash by night.

The reason that I did not start this chapter with a definition of ME is that there is no general accepted agreement on the definition of ME, or the pathophysiology of ME, or an accepted understanding of ME chronicity. Many doctors simply do not believe that ME exists except as one of various psychiatric or social disorders or as an Internet-constructed example of mass hysteria. One would think that this was bad enough, but it gets worse. There is disagreement as to whether ME and CFS represent the same disease spectrum. There are now thousands of scientific publications on ME and CFS, but those publications on physical dysfunction are much like the parable of the six blind men of Hindustan, who individually described the elephant as a wall, a spear, a snake, a tree, a rope and a fan. To my knowledge, since and including the 1932 ME epidemic in the LA County Hospital and the first excellent publication of that epidemic by AG Gilliam, no one has ever done a complete long-term systematic scientific study on any significant number of patients with ME or CFS. No wonder, then, that doctors and scientists are in disarray on ME and CFS. It is also obvious that many people diagnosed with ME and CFS are missed patients with multi-system, multi-organ pathology. Are these pathologies due to a specific CNS injury or generalized injuries acquired during the initial infectious, immunological, chemical or traumatic injuries, or are they genetically related illnesses? We simply do not know.

Nor is there any agreement as to whether ME⁵ represents the same disability as CFS.^{6,7} In the USA, the conflicting name for CFS is 'chronic fatigue and immune dysfunction syndrome' (CFIDS). In the UK, some doctors have used the term 'postviral syndrome' to describe ME. In addition to the above definitions, there are possibly better, more recent definitions, including the so-called 'Canadian definition'⁸ and the 'children's definitions' by Jason and colleagues.^{9,10} Unlike any other medical condition, real or imagined, I know of no other where there are two warring armies of very well-educated doctors who are so critical of the others' views on the subject as to whether this is a real or imagined illness or whether ME is the same as CFS. There should be no surprise when I tell you that there is no accepted agreement on the treatment of ME or CFS either. This treatment

quandary is particularly true if you examine the complexity of the pathologies hidden within the group of patients I have discussed above and whom well-educated doctors refer to as having ME and CFS. Let us briefly discuss the definitions.

Definitions of reputed infectious and other diseases come in various sizes and constructions, but essentially there are two types of definitions:

- *Epidemic-based definitions:* these are from the bottom up and are based upon epidemic findings when large groups of individuals fall ill at the same time, usually in confined quarters. The clarity of such a definition changes with technological and clinical advancements, particularly if a single causative agent is found. Physicians and researchers who investigate the epidemics always construct these definitions. These definitions, often faulty, at least have the benefit of being based on physical findings and follow-up of actual patient illness by doctors and scientists who investigate the actual patients over a period of time.
- *Theoretical-based definitions:* these are based on a theory of preconceived limits of what an illness is supposed to be and what is supposed to happen in the illness. They are often based upon symptoms rather than pathological findings. The Centers for Disease Control and Prevention (CDC) definitions of CFS are typical of this type of bureaucratic definition. This type of definition excludes all patients who do not follow this hypothetically derived definition. This type of definition is often bureaucratic, dictated from the top down, and those that direct this definitional process at times tend to have little and often no experience in primary patient investigation of the illness process that they are attempting to describe. Unfortunately, this is not unusual in medicine today. Since the same symptoms are often common to a multitude of different illnesses, these definitions tend to be misleading.

Why is the derivation of a definition important? Before Pierre Marie and Ivan Wickman's description of epidemic poliomyelitis based upon the first major poliomyelitis epidemics in 1887 and 1895 in Stockholm,^{11,12} what we now know as poliomyelitis was described under a multitude of different diseases, with multiple different names and different causes. Epidemic descriptions by clinical investigators with careful follow-up have the advantage of bringing together the multiple and varied aspects of a single illness. One eminent French neurologist in the 1890s described the Scandinavian polio epidemics discussed by Wickman as examples of mass hysteria, although he had never been to Scandinavia or examined any patient. It was only when doctors such as Wickman studied the outcome of the late nineteenth-century Scandinavian poliomyelitis epidemics that doctors and scientists were able to bring these previously multiple disease phenomenon together under one classification. Unfortunately, in none of the more than 60

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epidemics of ME has anyone thought to do a funded systematic pathophysiological investigation and long-term follow-up of these epidemic patients. This itself is perhaps the biggest tragedy.

Definitions of ME

Doctors and workers who studied patients during epidemics of ME developed the following definitions. The definitions were not good, since most were developed at a time when virology was in its infancy or later when scientific research was largely underfunded:

- *Onset and location:* these were acute, epidemic and concurrent endemic episodes that occurred in both children and adults starting in late summer and early autumn in the north temperate zone. Onset of new disease tended to decrease rapidly after October, finally trailing off during the Christmas–New Year period. Most frequently described epidemics occurred in schools, hospitals and military camps, particularly when associated with institutional residences and crowding. Increased endemic infection was often noted at the same time.
- *Symptoms:* the symptom picture is characterized by its acute explosive onset, the severity of the CNS, autonomic and vascular symptoms, the associated malaise, and the often fleeting muscle and joint pains, but with a paucity of physical signs on physical examination and very low death rate. Little is said about duration and long-term findings. In my experience, depending upon the individual case, after weeks, months or sometimes years, this acute symptom picture gradually decreases in intensity. However, the average patient's intellectual, physical and emotional stamina, whose decrease tended to be noticed within 2–4 weeks of illness onset, rarely recovers sufficiently for the patient to manage in the competitive world if the illness continues beyond 2 years. As in any true disease, there is variable severity and simply misdiagnosis.
- *Pathology:* the few deaths that went to autopsy demonstrated CNS injuries to the basal ganglia and other brain areas, and injuries to the anterior horn cells and dorsal root ganglia (A Chaudhuri, personal communication, February 2009). Unlike in paralytic poliomyelitis, the anterior horn cells tend to be injured rather than destroyed. Deaths occurred during and following the epidemics, including three children under 12 years of age who died of Parkinson's disease within 2 years of falling ill during the 1947 Iceland epidemic.
- *Clinical tests:* abnormal EEGs were found in the Royal Free epidemics.^{13,14} Abnormal electromyography (EMG) was found in the LA, Copenhagen, Royal Free and Coventry epidemics. Neurologist Charles Poser found oligoclonal banding in some sporadic cases in referred patients at Harvard's Mount Sinai Hospital,¹⁵ but he is perhaps the only doctor to have taken routine spinal

fluids. Oligoclonal banding suggests CNS injury. These were all earlier epidemics. Outside of our own work, to my knowledge little if any systematic investigation has been done of significant groups of patients in the multitude of post-1984 cluster, epidemic and endemic cases.

- *Cause:* in the more than 60 epidemics and clusters described, only in four was an infectious source actually recovered and described. In four of the instances, this virus was an enterovirus or ECHO enterovirus, which were recovered in the later Akureyri episodes,¹⁶ the Coventry epidemic¹⁷ and the Ottawa 1984 clusters by DN Galbraith and C Nairn of Ruckhill Hospital, Glasgow (unpublished investigations). In Ontario, the provincial virologists also observed an association only with enteroviruses during the 1984–90 epidemic periods¹⁸ and a negative association with Epstein–Barr virus (EBV). Concomitant gastrointestinal bacterial infection with Bethesda Ballerup paracolony group¹⁹ was isolated in some of the patients in the Bethesda outbreak. It was not believed to be a cause. John Chia in California has recovered enterovirus from the gastric mucosa in multiple sporadic ME patients whom he has investigated.²⁰ The great difficulty in recovering polio enteroviruses in living patients should be remembered; almost all polioviruses in patients with polio were recovered from autopsy cases.
- *Incubation period:* in the 60 or so described epidemics, when an observed incubation period was noted, in most cases they were stated as 3–6 days.²¹ Except for the 1934 LA epidemic, which was associated within days of immunization of the hospital staff, no other incidence of immunization association was specifically recorded. Most enteroviruses have an incubation period of 8–40 days, making EBV virus with a 40-day incubation period a highly unlikely cause of epidemic ME.

Definitions of CFS

These are definitions that started with the 1988 National Institutes of Health (NIH)/CDC Holmes definition.⁶ The important fact with regard to this definition is that only 2 of the 16 authors had routinely investigated patients with ME and published on ME or CFS before or after the publication. The 1988 definition was followed up by the 1991 Oxford Guidelines²² and the 1992 NIH/CDC Fukuda definitions, which at best were copies of the 1988 definition. These three definitions are examples of theoretical definitions and are not based upon significant patient examination. If anything, they served to confuse the severity of ME that was associated with the term CFS. The later, so-called Canadian definition⁸ is unique in the fact that the majority of the authors had long-term experience of examining patients with ME. This definition discusses many of the findings in this chapter. The definition is lacking in that it was not based significantly upon actual organ and system pathophysiology and examination. It does not distinguish

between ME and CFS. This definition is also much too long and complex; however, it remains the closest among the published definitions in describing the actual disease known as ME.

KEY POINTS

- ME occurs as an epidemic and endemic disease. The injured patients as a group have rarely been investigated systematically during the past 50 years with the force of modern scientific and clinical investigational tools. Doctors investigating the patient with ME have rarely if ever received any significant funds for in-depth scientific investigation of organ and system pathologies.
- ME epidemic patients as a group have never been subjected to any long-term follow-up. Grufferman has suggested the possibility of increased cancer risk in the cohorts of epidemic ME-type patients.²³
- ME and CFS are symptom-based definitions that have become simple garbage-bag terms for large numbers of patients with acute or gradual-onset physical and cognitive diseases affecting stamina, work and school ability. Thus, the terms ME and CFS have acted as an excuse to downplay the importance of these chronically ill patients and to not properly investigate these patients.
- The patient with ME has been largely disenfranchised from modern medical investigation and suitable medical assistance. Since most of these individuals tend to be relatively young, highly educated individuals in the medical and teaching professions, their loss of tax income to the government would more than offset their in-depth investigational costs.
- The majority of patients with ME or CFS that we have investigated in the UK, the USA or Canada represent multiple missed pathologies rather than any single disease entity. Whether these pathologies are caused by an initial CNS injury that deregulates the complex neuro-immune and neurochemical system and organ physiology of the patient or are simply co-morbidities is simply not known.
- There will never be a single treatment, whether pharmaceutical, physical, psychological or psychiatric, that will have any significant effect in the treatment of the majority of patients with ME and CFS, since they do not have a common trigger or common organ and system pathologies. It is necessary to first investigate the pathophysiological injuries and then treat them where possible to obtain a reasonable chance of a cure or treatment.
- The ME community continues to be a growing concern to many doctors and the state. This community is unlikely to disappear.
- Both patient and doctor mythologies continue to form a major part in the failure to assist the patient with ME.
- One group of patients with ME and CFS for whom we know their pathology – the patients with dysautonomia – have seen no advance in funding or investigation of treatment in the past 30 years, to such an extent that most major cities and university medical schools in the UK, Europe and North America simply have no investigational ability in this area.
- The major problems in understanding the illness and disability of patients with ME and CFS lie in the following areas: (i) the Oslerian concept of a single pathology causing a single disease spectrum; (ii)

the misguided notion that patients with ME and CFS are people who can 'think themselves sick'; (iii) the lack of funding and resources in the physical investigation into the pathologies and pathophysiologies of these patients; (iv) the failure to do any long-term follow-up study of this group of chronically ill patients; (v) the patient mythologies that magic treatments can cure the patient; and (vi) the erroneous and facile belief that patients with ME and CFS simply have variations of hysteria, somatization disorders or somatoform disorders in general.

The fault, dear reader, is not in our stars nor among the doctors or the patients, but in the system in which these two often apposing forces, the doctor and patient, theory and scientific investigation, exist. Until we actually do systematic long-term and in-depth scientific investigation of these patients, we will see no progress. Until then, I can only recommend that the doctor offers kindness to and toleration of these chronically disabled largely mistreated patients with ME and CFS. To the government of the UK, I can only recommend the nationwide funding of a serious scientific approach to the long-term pathophysiological investigation of these chronically disabled citizens.

And we 'remain' as on a darkling plain

Swept with confused alarms of struggle and flight,

Where ignorant armies clash by night.

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