

Lyndonville News

Volume 1, Number 3: October 2004

Information and Support for the ME/CFS/FM Community
David S. Bell MD, FAAP, Editor

DavidSBell.Com

DEFINITIONS OF AN ILLNESS

Please note the change in address for the newsletter. Thanks to Carrie Patten and Fireside Design Studio we now have a web site, and the Lyndonville News will be e-mailed from that site.

The e-mail subscription continues to be free but may not have nice pictures or graphics. Therefore, you may want to consider the hard copy instead of the e-mail version mailed to your house. That way you can fix a nice cup of tea, relax in your easy chair, then read at leisure and look at the pictures instead of staring at an annoying computer screen, making your headache worse. If you want the hard copy, you can send \$20 for one year to D. S. Bell, MD, 77 South Main Street, PO Box 495, Lyndonville, NY 14098. The down side of this is that if I give up the newsletter tomorrow you are out twenty bucks. So much for my earlier promise to be commercial free.

Introduction

Welcome to the third edition of the Lyndonville News. I would like to thank those of you who have provided feedback, and one change we will make is to cluster the articles around a specific topic, and in this edition we will discuss illness definitions, including the definitions of ME from Dr. Ramsay, and orthostatic intolerance. This is a topic which can inflame the passions of many with ME/CFS/FM as it is central to the identity of the illness, and thus central to the issues surrounding the respect, dignity and integrity of the patient. Do we call it dysautonomia, ME/CFS/FM, neuroendocrineimmune dysfunction, postural tachycardia and so on.

One of my greatest hopes is that by the time I am so old as to not be able to write a newsletter anymore, this illness will have solved its identity crisis. The umbrella term would be such-and-such, and the subtypes would include...

Presently chronic fatigue syndrome is the umbrella term used by most practitioners in this country. The benefit is that some patients are getting a correct diagnosis and are being treated with respect. The drawback of course is that it is a lousy name and engenders societal disrespect and Jay Leno jokes. My own contribution to this identity crisis in this newsletter is to call it

ME/CFS/FM. We will be starting off with one of the original descriptions of the illness by Dr. Melvin Ramsay.

Guest Editorial: Jean Harrison, MAME

Dr. Melvin Ramsay, 1901-1990. Dr. Ramsay's contribution to the study of ME/CFS would be hard to overstate. A specialist in infectious diseases, he was working at the Royal Free Hospital in London in 1955 when more than 200 people were stricken with what he recognised to be a disease of infectious origin. Indeed nearly 300 exhibited signs of illness, but he was convinced that about 90 of those had an hysterical reaction to watching their colleagues fall ill so suddenly and dramatically. It was through his work that a host of disease outbreaks which at that time had been given different names were most likely the same illness, an illness which in 1956 became known as myalgic encephalomyelitis (ME). He adopted a set of diagnostic criteria for the disease and observed that "Myalgic Encephalomyelitis is an endemic illness with epidemic periodicity" (Hyde et al, 1992 p 82) and also noted that the disease was similar in many aspects to non-paralytic poliomyelitis. Had his work been better known at the time of the US epidemics of the 1980's the course of study of the illness would, most likely, have been much more beneficial to the patients. He had no doubt that ME was an extremely serious illness.

History

MYALGIC ENCEPHALOMYELITIS : A Baffling Syndrome With a Tragic Aftermath.

By A. Melvin Ramsay M.D., Hon Consultant Physician, Infectious Diseases Dept, Royal Free Hospital. 1986

The syndrome which is currently known as Myalgic Encephalomyelitis in the UK and Epidemic Neuromyasthenia in the USA leaves a chronic aftermath of debility in a large number of cases. The degree of physical incapacity varies greatly, but the dominant clinical feature of profound fatigue is directly related to the length of time the patient persists in physical effort after its onset; put in another way, those patients who are given a period of enforced rest from the onset have the best prognosis.

Although the onset of the disease may be sudden and without apparent cause, as in those whose first intimation of illness is an alarming attack of acute vertigo, there is practically always a history of recent virus infection associated with upper respiratory tract symptoms though occasionally there is gastrointestinal upset with nausea and vomiting. Instead of making a normal recovery, the patient is dogged by persistent profound fatigue accompanied by a medley of symptoms such as headache, attacks of giddiness, neck pain, muscle weakness, parasthesiae, frequency of micturition or retention, blurred vision and/or diplopia and a general sense of 'feeling awful'. Many patients report the occurrence of fainting attacks which abate after a small meal or even a biscuit, and in an outbreak in Finchley, London, in 1964 three patients were admitted to hospital in an unconscious state presumably as a result of acute hypoglycaemia. There is usually a low-grade pyrexia which quickly subsides. Respiratory symptoms such as sore throat tend to persist or recur at intervals. Routine physical examination and the ordinary run of

laboratory investigations usually prove negative and the patient is then often referred for psychiatric opinion. In my experience this seldom proves helpful and is often harmful; it is a fact that a few psychiatrists have referred the patient back with a note saying 'this patient's problem does not come within my field'. Nevertheless, by this time the unfortunate patient has acquired the label of 'neurosis' or 'personality disorder' and may be regarded by both doctor and relatives as a chronic nuisance. We have records of three patients in whom the disbelief of their doctors and relatives led to suicide; one of these was a young man of 22 years of age.

The too facile assumption that such an entity - despite a long series of cases extending over several decades - can be attributed to psychological stress is simply untenable. Although the aetiological factor or factors have yet to be established, there are good grounds for postulating that persistent virus infection could be responsible. It is fully accepted that viruses such as herpes simplex and varicella-zoster remain in the tissues from the time of the initial invasion and can be isolated from nerve ganglia post-mortem; to these may be added measles virus, the persistence of which is responsible for subacute sclerosing panencephalitis that may appear several years after the attack and there is a considerable body of circumstantial evidence associating the virus with multiple sclerosis. There should surely be no difficulty in considering the possibility that other viruses may also persist in the tissues. In recent years routine antibody tests on patients suffering from myalgic encephalomyelitis have shown raised titres to Cocksackie B Group viruses. It is fully established that these viruses are the aetiological agents of 'Epidemic Myalgia' or 'Bornholm's Disease' and that, together with ECHO viruses, they comprise the commonest known virus invaders of the central nervous system. This must not be taken to imply that Cocksackie viruses are the sole agents of myalgic encephalomyelitis since any generalised virus infection may be followed by a period of post-viral debility. Indeed, the particular invading microbial agent is probably not the most important factor. Recent work suggests that the key to the problem is likely to be found in the abnormal immunological response of the patient to the organism.

A second group of clinical features found in patients suffering from myalgic encephalomyelitis would seem to indicate circulatory disorder. Practically without exception they complain of coldness in the extremities and many are found to have abnormally low temperatures of 94 or 95 degrees F. In a few, these are accompanied by bouts of severe sweating even to the extent of waking during the night lying in a pool of water. A ghostly facial pallor is a well known phenomenon and this has often been detected by relatives some 30 minutes before the patient complains of being ill.

The third component of the diagnostic triad of myalgic encephalomyelitis relates to cerebral activity. Impairment of memory and inability to concentrate are features in every case. Many report difficulty in saying the right word and are conscious of the fact that they continue to say the wrong one, for example 'cold' when they mean 'hot'. Others find that they start a sentence but cannot complete it, while some others have difficulty comprehending the written or spoken word. A complaint of acute hyperacusis is not infrequent; this can be quite intolerable but alternates with periods of normal hearing or actual deafness. Vivid dreams generally in colour are reported by persons with no previous experience of such a phenomenon. Emotional lability is often a feature in a person of previous stable personality, while sudden bouts of uncontrollable

weeping may occur. Impairment of judgment and insight in severe cases completes the 'encephalitic' component of the syndrome.

I would like to suggest that in all patients suffering from chronic debility for which a satisfactory explanation is not forthcoming a renewed and much closer appraisal of their symptoms should be made. This applies particularly to the dominant clinical feature of profound fatigue. While it is true that there is considerable variation in degree from one day to the next or from one time of the day to another, nevertheless in those patients whose dynamic or conscientious temperaments urge them to continue effort despite profound malaise or in those who, on the false assumption of 'neurosis', have been exhorted to 'snap out of it' and 'take plenty of exercise' the condition finally results in a state of constant exhaustion. This has been amply borne out by a series of painstaking and meticulous studies carried out by a consultant in physical medicine, himself an ME sufferer for 25 years. These show clearly that recovery of muscle power after exertion is unduly prolonged. After moderate exercise, from which a normal person would recover with nothing more than a good night's rest, an ME patient will require at least 2 to 3 days while after more strenuous exercise the period can be prolonged to 2 or 3 weeks or more. Moreover, if during this recovery phase, there is a further expenditure of energy the effect is cumulative and this is responsible for the unrelieved sense of exhaustion and depression which characterises the chronic case. The greatest degree of muscle weakness is likely to be found in those muscles which are most in use; thus in right-handed persons the muscles of the left hand and arm are found to be stronger than those on the right. Muscle weakness is almost certainly responsible for the delay in accommodation which gives rise to blurred vision and for the characteristic feature of all chronic cases, namely a proneness to drop articles altogether with clumsiness in performing quite simple maneuvers; the constant dribbling of saliva which is also a feature of chronic cases is due to weakness of the masseter muscles. In some cases, the myalgic element is obvious but in others a careful palpitation of all muscles will often reveal unsuspected minute foci of acute tenderness; these are to be found particularly in the trapezii, gastrocnemii and abdominal rectii muscles.

The clinical picture of myalgic encephalomyelitis has much in common with that of multiple sclerosis but, unlike the latter, the disease is not progressive and the prognosis should therefore be relatively good. However, this is largely dependent on the management of the patient in the early stages of the illness. Those who are given complete rest from the onset do well and this was illustrated by the aforementioned three patients admitted to hospital in an unconscious state; all three recovered completely. Those whose circumstances make adequate rest periods impossible are at a distinct disadvantage, but no effort should be spared to give them the all-essential basis for successful treatment. Since the limitations which the disease imposes vary considerably from case to case, the responsibility for determining these rests upon the patient. Once these are ascertained the patient is advised to fashion a pattern of living that comes well within them. Any excessive physical or mental stress is likely to precipitate a relapse.

It can be said that a long-term research project into the cause of this disease has been launched and there are good grounds for believing that this will demonstrate beyond doubt that this condition is organically determined.

Literature Review

Schondorf R, Freeman R. *The Importance of orthostatic intolerance in chronic fatigue syndrome*. Am J Med Sci 1999;317(2):117-123.

Even though this paper is already old, I think it has importance, particularly for our discussions related to the definitions of the illness. The paper starts with standard definitions of CFS and of orthostatic intolerance (OI). “Symptoms of orthostatic intolerance, such as disabling fatigue, dizziness, diminished concentration, tremulousness, and nausea, are found in patients with CFS.” Furthermore they explain that patients with orthostatic intolerance do not have florid autonomic failure.

“Certain features of CFS bear a strong resemblance to those of postural tachycardia syndrome (POTS)” The strict diagnosis of orthostatic intolerance in this paper is said to be “inability to maintain consciousness in the upright position.” Tilt table testing requires either syncope or presyncope. Overall the authors here feel that between 25% and 40% of patients with CFS have a defined type of orthostatic intolerance.

Treatment is discussed in terms of physical interventions (position, stockings, etc), volume expansion with sodium or fludrocortisone as well as alpha-adrenergic analogs (midodrine).

Comment: While this paper is to be praised in attempting to link CFS with orthostatic intolerance, it fails by saying that CFS symptoms occur in some persons with OI. They allow the diagnosis of OI only with the defined abnormalities on tilt table testing, and not the symptom of inability to maintain the upright position, which is the central feature of both CFS and all forms of orthostatic intolerance.

Clinical Notes:

The Symptom of Orthostatic Intolerance in Chronic Fatigue Syndrome

Chronic Fatigue Syndrome (CFS) is a multi-symptom illness with a wide range of severity, able to cause significant disability. For an excellent comprehensive review please see John & Oleske (1). The illness has been surrounded in controversy for years, particularly because the degree of disability is not predicted by the relatively normal physical examination and routine laboratory findings. Even the name “chronic fatigue syndrome,” contributes to the controversy by implying that simple fatigue or tiredness is the central disabling symptom. In this paper, I would like to suggest that the central and most disabling symptom of CFS is not fatigue but the symptom of orthostatic intolerance.

Disability is defined as an alteration of an individual’s capacity to meet personal, social, or occupational demands because of an impairment (2). Criteria for the research diagnosis of CFS were first published in 1988 (3) and revised in 1994 (4) and again recently (5). Essentially, these

criteria require a new onset of activity limiting fatigue which is not caused by ongoing exertion and is not relieved by appropriate rest. Thus, by definition, CFS requires at least some degree of disability. Patients must also have at least four of the following eight symptoms: cognitive dysfunction; recurrent sore throat; tender cervical or axillary lymph nodes; muscle pain; multi-joint pain; headache of new pattern; unrefreshing sleep; and post exertional malaise lasting more than twenty-four hours. Criteria published by the Canadian consensus panel (6) describe ME/CFS in more detail and include orthostatic intolerance.

For those patients unable to work or attend school due to CFS, they express difficulty in explaining the exact reason, other than to say they “feel too sick.” Of course, employers or schools have a difficult time understanding, as illness is generally expected to resolve within a short time. It is the use of the term ‘fatigue’ that causes the greatest confusion in regard to disability status. Technically, fatigue is a state of recovery, and this does not occur in persons with CFS. Occupational medicine physicians may argue that it is appropriate to work with fatigue, with the assumption that normal fatigue, like normal muscle weakness, will respond to increased activity. While this is appropriate for normal fatigue, it is usually not the case with CFS.

The symptom of fatigue as experienced in CFS is quite different from the shared common experience of fatigue. Patients use several terms in an attempt to describe this symptom, including “weakness”, “heaviness”, “exhaustion”, and “sleepiness”. This experienced sensation is better served by the term ‘orthostatic intolerance’ meaning limitation of sustained upright activity. Orthostatic intolerance is defined as the inability to tolerate, over time, the upright position, either sitting, standing, or walking. The symptoms are at least partially relieved by recumbency.(7)

The term orthostatic intolerance is used in two ways: it is a symptom confused with simple fatigue, and it is an umbrella term for more specifically defined conditions such as postural orthostatic tachycardia, orthostatic hypotension, delayed orthostatic hypotension, neurally mediated hypotension, and orthostatic narrowing of the pulse pressure. Abnormalities in the autonomic nervous system underlie both the symptom of orthostatic intolerance and its defined subtypes, and is an active area of current research.

The symptom of orthostatic intolerance causing limitation of sustained upright activity is the central disabling symptom of CFS. After a period of time in the upright position, a person with CFS becomes overwhelmed with “fatigue,” pain, confusion and other symptoms requiring the patient to lie down. Symptoms such as sore throat, lymph node pain, muscle and joint pain are not in themselves orthostatic, but in my experience, are exacerbated by prolonged standing or sitting. I feel that the cognitive symptoms of CFS are orthostatic in nature, but this has not been tested.

In CFS, activities such as light walking may be better tolerated than quiet standing, most likely because of the circulatory effects of muscle contraction. However, even these activities are limited in persons with CFS. In general, sitting is better tolerated than standing, but both are considered orthostatic stress. The symptom of worsening or malaise after exertion in the

diagnostic criteria (4) is caused primarily by orthostatic stress. Recumbency, with or without sleep, is the action which relieves this discomfort.

As a symptom, orthostatic intolerance may be described just as any other symptom. Proof of the existence of this symptom is always difficult, just as the presence of pain is difficult to prove. Attempts to prove orthostatic intolerance with a tilt table has lead to categorization of the subtypes described above. However, persons with CFS may have a normal tilt table test despite severe symptomatic orthostatic intolerance (8). It is for this reason that quiet standing in the office with behavioral observations combined with pulse and blood pressure monitoring has been suggested and normal values established (9). Furthermore, quiet standing more closely resembles normal or daily orthostatic stress.

The misunderstandings surrounding CFS have led to substantial suffering of patients over and above the symptoms imposed by the illness. One potential way for these misunderstandings to be addressed is to employ the more accurate term of orthostatic intolerance to describe the central disabling symptom of the illness.

References

1. John JJ, Oleske, eds. *A Consensus Manual for the Primary Care & Management of Chronic Fatigue Syndrome*, The Academy of Medicine of New Jersey & The New Jersey Department of Health and Senior Services, Lawrenceville, NJ, 2002.
2. American Medical Association. *Guide to the Evaluation of Permanent Impairment*. 5th ed. Chicago Ill, 1995.
3. Holmes GP, Kaplan JE, Gantz NA, et al. *Chronic fatigue syndrome, a working case definition*. *Anhn Intern Med* 1988;108:387-389.
4. Fukuda K, Straus SE, Hickie I, et al. International Chronic Fatigue Syndrome Study Group. *The chronic fatigue syndrome: a comprehensive approach to its definition and study*. *Ann Intern Med*. 1994;121:953-959.
5. Reeves WC, Lloyd A, Vernon SD, Klimas N, Jason LA, Bleijenberg G, Evengard B, White PD, Nisenbaum R, Unger ER, et al. *Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution*. 2003;BMC Health Services Research. 2003;3:25.
6. Carruthers B, Jain A, DeMeirlier K, Peterson D, Klimas N, Lerner A, et al. *Myalgic encephalomyelitis/chronic fatigue syndrome: Clinical working case definition*. diagnostic and treatment protocols. *J Chronic Fatigue Syndrome*. 2003;11(1):1-12.
7. Stewart J. *Orthostatic intolerance: a review with application to the chronic fatigue syndrome*. *J Chronic Fatigue Syndrome*. 2001;8:45-64.
8. Gerrity TR, Bates J, Bell DS, Chrousos G, Furst G, Hedrick T, Hurwitz B, Kula RW, Levine SM, Moore RC, Schondorf R. *Chronic fatigue syndrome: what role does the autonomic nervous system play in the pathophysiology of this complex illness?* *Neuroimmunomodulation*. 2002-3;10:134-141.
9. Stewart JM. *Orthostatic intolerance: A review with application to chronic fatigue syndrome*. *JCFS*. 2001; 8:45-64.
10. Streeten DH. *Orthostatic Disorders of the Circulation*. New York. Plenum 1987:116.

Question and Answer

“In your last newsletter you wrote about two research studies. One found that 53.3% of CFS patients tested positive for a certain autoantibody....my fear is that this study, as in so many studies that you read about, will be dismissed because it does not provide a marker for CFS. It seems to me that when they find positive results like this, then the thing to do is to find other people with the same positive test and group them together and call that one disease. I have never seen this done. My question is: why?”

Thanks for the question. And it pinpoints the current dilemma that the CFS research community finds itself in. How can we break ME/CFS/FM down into meaningful groupings? Lets take this example: There are fifty persons with fever, cough, and abnormal chest x-ray. There are numerous germs measured in these fifty persons, including viruses, bacteria, and other organisms. In an attempt to determine what to call this illness, many studies have been done, and it turns out that of the fifty, forty were born in New York state. Aside from being somewhat unlucky for them, does this detail have any importance, or help in defining this disease? The answer to this question is that the fifty persons have pneumonia, and the detail that some were born in New York state is irrelevant.

But subgrouping is exactly what we are trying to do with CFS. There are several potential subgroups that come to mind: 1) acute vs gradual onset; 2) severe neurologic symptoms vs milder neuro symptoms; 3) presence of “viral” type symptoms (sore throat and lymph node pain) vs absence of “viral” symptoms; presence of markers such as RNase-L and so on. The problem is that when we look at specific groups, instead of nice crisp groups, the edges begin to blur.

Take the separation of CFS from fibromyalgia (FM) for example. In the early eighties they were considered two distinct illnesses. FM was seen by the rheumatologists and CFS was seen by the infectious disease specialists. But when the studies started coming in, the Epstein-Barr virus titers did not help to separate them into different groups, nor did the immunology, nor even the symptom pattern as it all crossed the lines. Now it seems that both the pain of FM and the exhaustion of CFS are due to the autonomic nervous system. One of the reasons that the work of Dr. Spence and colleagues is so valuable is that they may have come across a clear physiologic difference between FM and CFS. We will return to this point in later editions of the newsletter.

In the study referred to in the question, it would be wonderful if discrete subtypes of ME/CFS/FM evolved from autoantibody tests. But this will require several studies with different laboratories for confirmation. In the past, this confirmation has not come. Epstein-Barr virus antibodies, for example, may be as irrelevant as being born in New York state. But who knows? Maybe autoantibodies will be the needed break. Time will tell.

Disclaimer Any medical advice that is presented in the Lyndonville News is generic and for general informational purposes only. ME/CFS/FM is an extremely complex illness and specific advice may not be appropriate for an individual with this illness. Therefore, should you be interested or wish to pursue any of the ideas presented here, please discuss them with your personal physician.