CONFIRMATION OF THE SIMILARITIES BETWEEN MYALGIC ENCEPHALOMYELITIS AND THE POST-POLIO SYNDROME

Our experience with myalgic encephalomyelitis (ME) leads us to believe ME not to be psychiatric but organic in origin and effect: consequently we have previously taken issue (1) with a much-published British psychiatrist, Dr Simon Wessely, who regularly and vigorously promotes his own view that ME is merely "the extreme end of a continuum that begins with the common feeling of tiredness" (2); that ME is nothing more than "a belief" (3); that he agrees with the view that "the average doctor will see (that ME patients) are neurotic and he will often be disgusted with them" (4) and that in "patients diagnosed as having.....myalgic encephalo-myelitis, the usual findings of simulated weakness were present" (5).

Especially unsatisfactory in our view is Wessely's repeated failure to distinguish between 'true' ME and degrees of generalised fatigue (6); he persists in addressing all fatigue states as an undifferentiated "Chronic Fatigue Syndrome", whilst we and others believe the use of this all-encompassing term "CFS", together with the failure to distinguish ME from CFS, serves only to obfuscate the necessary distinction between the conditions. To this end, we entirely agree with the UK findings that progress in understanding these syndromes is hampered by the invalid comparison of contradictory research findings stemming from the use of hetergeneous study groups which have used divergent selection criteria (7).

We believe such obfuscation can only be harmful to those whose diagnosis is not CFS but ME; but so unduly keen does Wessely seem in the promotion of his own beliefs that he has even challenged the World Health Organisation classification of ME as a neurological disease (International Classification of Diseases 10: G 93.3) by writing in The Lancet that "Neurasthenia would readily suffice for ME..... applying more stringent criteria for CFS in the hope of revealing a more neurological subgroup succeeds only in strengthening the association with psychiatric disorders..... We believe this latest attempt to classify fatigue syndromes will prevent many people from seeing the world as it actually is" (8).

More recently, a nurse who works with Wessely has written a book (Chalder,T: Coping with Chronic Fatigue. London: Sheldon Press, 1994, 70pp) in which she promotes the use of cognitive behavioural therapy (CBT), for example stating on page 20 "following what your body tells you can do more harm than good", and on page 33 "the key to success lies in increasing your level of activity gradually and consistently". Given that Wessely and colleagues have devised a form of CBT which assumes that the fatigue associated with CFS is not a symptom of on-going disease,(9) inevitably Wessely claims in his preface to this book that this approach is "practical, useful and effective".

However, we now draw strength from a recently published volume (10),and believe that as a result of this publication, it may well be time for Wessely to consider re-appraising his position about the validity of ME as a nosological entity.

This prestigious tome contains the proceedings of the first international scientific conference on the Post-Polio Syndrome (PPS) from the Annals of the New York Accademy of Sciences 1995,; it contains 50 papers written by 118 contributors from a wide range of specialities, including Clinical Neurology, Neuroscience, Electrophysiology, Brain imaging, Histology, Virology, Immunology, Epidemiology and Rehabilitation, with most of the contributors coming from the USA but including participants from Australia, Canada, France, Sweden and the UK.

Importantly, there are several papers which point out the similarities between post-polio syndrome and ME, as well as with other known enteroviral diseases such as Motor Neuron Disease; significantly, it appears that the **mechanism** of the extreme fatigue (called here "visceral exhaustion") is **exactly** the same in ME as the mechanism which is described in PPS.

In particular, the paper by Bruno et al from the Department of Physical Medicine and Rehabilitation, New Jersey Medical School (11) has many useful comparisons of ME with PPS, for instance, the authors state "these relationships and recent empirical comparisons will be described" (page 259); they then deal with the similarities and association of ME with **Atypical Poliomyelitis** dating from 1934, and then consider the more direct association between **Type III Poliovirus** and ME. Discussing the latter, the authors state "More recent support for a relationship between Poliovirus and ME came in 1989 when a 'dangerously rising titre' to type III Poliovirus was documented in a patient (who) had been diagnosed with ME".

It is noteworthy that these authors differentiate between ME and CFS: in comparing post-polio fatigue and CFS, they note that "85% of patients with CFS demostrated "an excess of irregular slow wave activity on EEG similar to that seen following ME and polio".

This same paper by Bruno et al continues "Some of the subjective difficulties with attention and cognition in CFS patients and polio survivors have been corroborated by the documentation of clinical abnormalities on neuropsychologic testing"; in discussing neuroanatomic studies in PPS patients, the authors note that the presence of hyperintense signal (HS) on MRI was "significantly correlated with fatigue severity.....**but not with depressive symptoms**".

They contiue "This notion is supported by a number of studies that have documented a relationship between HS, impaired attention, and fatigue. Notably, periventricular and deep white (but not grey) matter HS have been imaged in between 40 and 100% of CFS patients and have been suggested to represent either enlarged, fluid-filled spaces around arterioles or demyelination".

Referring to the relationship between hypothalamic - pituitary- adrenal axis activit and the symptoms of (post-polio) fatigue, findings of significant negative correlations between ACTH levels and fatigue severity, cognitive problems and difficulty staying awake suggest that a diminution in HPA hormones may contribute to the symptoms of post-polio fatigue; moreover Bruno et al observe that "decreased HPA activity has already been documented in patients with CFS and the reduced secretion of "activating" peptides such as CRH and ACTH has been implicated in its pathophysiology".

Interestingly, they observe that "a reduction in βendorphin and enkephalin production might help to explain polio survivors' nearly doubled sensitivity to pain", a finding which is so familiar in ME.

Fatigue of central origin and its differentiation from muscle fatigue is a major concern expressed in several conference papers, but the Bruno paper is the most detailed. This paper shows that the clinically dominant "central fatigue" arises from neuronal damage in the mid-brain, especially affecting the reticular activating system (RAS), the function of which is to alert the cerebral cortex to ascending sensory information and to maintain wakefulness and attention. The resulting drowsiness, fatigue, fleeting attention and cognitive disturbances have been noted to affect many children after the symptoms of acute poliomyelitis have cleared, and that they are similar to, but less prolonged and chronic than analogous problems arising in ME, multiple sclerosis and post-encephalitic Parkinsonism.

These same authors particularly note that "polio survivors report that they are most distressed and disabled by the "visceral" symptoms of fatigue (and) feelings of exhaustion " which generate in the sufferer avoidance of physical activity: they point out, however, that "there would be survival value in a brain mechanism that monitors cortical activation and biases the organism toward cessation of motor behaviour and promotes rest when attention and information processing ability are impaired".

The paper by Bartfeld et al (12) from New York University Medical Centre is another which draws comparisons between post viral fatigue syndrome and PPS. They state "Consistent with a persistent viral infection is the fatigue noted by PPS patients and similar findings in a small number of patients with post viral fatigue syndrome. In PPS, characterisation of the RNA fragments suggests the absence of a complete viral genome. Attemps at subtyping have suggested either a relationship to Coxsackie virus or the presence of a large number of genomic mutations of poliovirus or other enteroviruses.....the ability to detect such material is greatly influenced by the virus subtype, mutations or defectivene level or expression and / or its focal distribution.....A translation product of such viral fragments may also trigger the immune-mediated inflammatory response witnessed in many PPS patients.....Persistent inflammation would result from an immune-mediated inflamma tory response to viral antigens encoded by non-infectious viral RNA fragments".

Another paper of relevance to ME is that by Muir et al (13) from StThomas' Hospita London: whilst it has long been known that enteroviruses cause persistent infections that may involve the central nervous system (CNS) in domestic and laboratory animals, this paper by Muir et al is outstanding in presenting new evidence, viz: "These studies provide virological evidence that enteroviruses may persist in the CNS of **man**".

The authors note "The presence of enterovirus RNA in serum or peripheral lymphocytes does not necessarily indicate CNS involvement and has been reported in patients.....with chronic fatigue syndrome. In the present study, a diagnosis of CFS was suspected in the one patient in whom enterovirus RNA was detected only in serum". They continue "The detection of viral RNA in cerebrospinal fluid is perhaps more surprising (and) may be analogous to findings described by Yousef et al (14) who cultured enteroviruses from the stools of patients with CFS only after acid dissociation of antibody-complexed virus".

In all, three separate groups of virologists, from the USA (NIH), UK (St Thomas' Hospital London) and France (Institut Pasteur) have found fragments of enterovirus RNA in the spinal cord and cerebrospinal fluid of some patients with PPS, suggesting that it could be caused by a superinfection with enterovirus such as Coxsackie.

Other papers devoted to Immunology and Virology suggest that damaged neurons, which later recover, may harbour enteroviral RNA fragments which are able to withstand immunological challenge.

Several papers comment on the role of **exercise** in rehabilitation: Agre (15) from the Department of Rehabilitation Medicine, University of Wisconsin, states that while exercise may improve muscle strength, cardio-respiratory function and ambulation, it is only beneficial if undue fatigue, muscle and joint pain do not occur during or after the exertion; Bruno et al (11) state that "the danger exists that a pharmacologic treatment for fatigue will allow (patients)

to resume their.....lifestyles.....and further stress....."metabolically vulnerable" neurons in the brain stem and anterior horn". Agre further states categorically that it is essential to ensure that improvement of function does not lead to overuse problems: most patients with ME know this, and have been saying so to their doubting physicians for years.

There are important and instructive papers on dysphagia, laryngospasm and speech difficulties, which also occur commonly in ME, and which are too often dismissed as hysterical in origin.

In conclusion, we again quote from the paper by Bruno et al (11): "Taken together, the historical, clinical and empirical findings presented above suggest a model for the pathophsyiology of post-polio fatigue.....neuroradiologic and neuroendocrine data have indicated damage to brain areas responsible for cortical activation and attention in polio survivors **and others with chronic fatigue".**

We hope this short review may help in lesening sufferes' additional burden of despair caused by the insults arising **not** from the disease process, but from medical ignorance and arrogance about the disease process.

We are encouraged to know that patients and researchers have once again gained respect and support, and that interest in enteroviral disease and its association with the major chronic neurological diseases of the 20th century has re-emerged, resulting, dare we hope, in less denigration of sufferers' afflictions caused by wrongful and unproven psychiatric attribution.

REFERENCES

1. MarshallE, Williams M: "The Views of Dr Simon Wessely on ME:Scientific Misconduct in the Selection and Presentation of Available evidence?". CFIDS Chronicle, Spring 1994: 14-18

2. Lewis G, Wessely S:"The epidemiology of fatigue: more questions than answers". Joural of Epidemiology and Community Health 1992:46:92-97

3. L.M.Howard & S.Wessely: "Psychiatry in the allergy clinic: the nature and management of patients with non-allergic symptoms". Clinical and Experimental Allergy 1995:25:503-514

4. Wessely S: Chronic fatigue and myalgia syndromes. In: N.Sartorius et al (eds): Psychological disorders in General Medical settings. Hogrefe and Huber 1990

5. Wessely S, Thomas PK: The chronic fatigue syndrome -- myalgic encephalomyelitis or postviral fatigue. In: C.Kennard (ed) Recent advances in Clinical Neurology No.6. Churchill Livingstone 1990:85 - 132

6. Marshall E, Williams M: Letter: CFIDS Chronicle Summer 1995:70

7. Report from the National Task Force on CFS/PVFS/ME sponsored by the UK Department of Health / Westcare, Bristol BS8 2RE: September 1994:1-133

8.David A, Wessely S: Chronic fatigue, ME and ICD 10: The Lancet, 13 November 1993:1247-8

9.ME/CFIFS Medical updates/Book Reviews Summer 1995

10.The Post-Polio Syndrome: Advances in the Pathogenesis and Treatment. (Dalakas MC,Bartfeld H, & Kurland LT:eds: Proceedings of the First International Scientific Conference on the Post-Polio Syndrome: Annals of the New York Academy of Sciences, vol.753: 1-409 (1995)

11. Richard L Bruno et al: "Pathophysiology of a Central Cause of Post-Polio Fatigue: ibid 257-275

12. Harry Bartfeld et al: "Relevance of the Post-polio Syndrome to other Motor Neuron Diseases: relevance to viral (Enteroviral) Infections". ibid:237-244

13. P. Muir et al: Evidnece for Persistent Enterovirus infection of the Central Nervous System in Patients with Previous Paralytic Poliomyelitis": ibid 219 -232

14. Yousef,G.E. et al: Chronic enterovirus infection in patients with postviral fatigue syndrome. The Lancet: 1988:i:146-150

15. James C Agre: The Role of Exercise in the Patient with Post-Polio Syndrome. (as ref. 10: pages 321 -

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