

## **“Where is the evidence that there is a need for careful sub-grouping within “CFS”?”**

There is now an unmistakable recognition that sound research has strengthened the need for consideration of subgroups. [\[1\]](#) [\[2\]](#) [\[3\]](#) [\[4\]](#) [\[5\]](#) [\[6\]](#) [\[7\]](#) [\[8\]](#)

A recent Editorial in the Journal of Chronic Fatigue Syndrome [\[9\]](#) makes the point that *“the sorting of patients into subpopulations....is helping in the design and interpretation of clinical trials for therapeutic interventions aimed at particular disease manifestations”*.

The 1994 CDC criteria for CFS (whilst referring only to CFS) themselves recommend that researchers use stratification techniques to identify subgroups of patients. [\[10\]](#)

One clear message which emerged from the National Institutes of Health (NIH) State of the Science Conference on CFS held on 23-24 October 2000 in Arlington, Virginia was that CFS is heterogeneous and researchers ***must*** subgroup patients by features including chronicity, immunology and neuroendocrinology. [\[11\]](#) Conference participants included Dr David Bell, Professor Dedra Buchwald and Professor Nancy Klimas, all world-renowned experts on CFS.

Roberto Patarca-Montero, Assistant Professor of Medicine and Director of the Laboratory of Clinical Immunology, University of Miami School of Medicine (as well as Editor of The Journal of Chronic Fatigue Syndrome) emphasises the importance of subsets of patients in his paper “Directions in Immunotherapy”. [\[12\]](#)

Experienced researchers and clinicians presented evidence at the Fifth International AACFS Conference held in Seattle, 27-29 January 2001 about the need for subgrouping. Some examples include the following:

--- Professor Leonard Jason from De Paul University, Chicago, concluded that *“Subtype differences detected may account for some of the inconsistencies in findings across prior studies that have grouped CFS patients into one category. Subtyping patients according to more homogeneous groups may result in more consistent findings which can then be used to more appropriately and sensitively treat the wide range of illness experience reported by different types of individuals with CFS”* [\[13\]](#)

--- Professor Kenny de Meirleir from Brussels compared immunological profiles in three different subgroups of CFS patients; he found significant differences between the groups. [\[14\]](#)

--- Dr Pascale de Becker from Brussels presented evidence that there is a need to assess the homogeneity of a large CFS population in order to establish those symptoms which can improve differentiation of CFS patients. [\[15\]](#)

--- Dr Paul Levine from Washington demonstrated that factor analysis is an important tool for separating subgroups of CFS; he showed that it should be utilised in future

attempts to develop case definitions for CFS to identify discrete patient groups, which may have different pathogeneses and responses to treatment. [\[16\]](#)

--- Dr Katherine Rowe from Australia presented evidence showing that at least three distinct subgroups can be identified within the CFS syndrome. [\[17\]](#)

--- A large international multicentre study of autoimmunity was presented by E.Tan (with, amongst others, participants from The Scripps Research Institute, La Jolla, California; the University of Washington; Harvard Medical School, Boston; State University of New York and George Washington University, Washington DC. Of interest is that another participant was Simon Wessely from Kings College, London). This large study reflected the heterogeneity from one CFS centre to another; it emphasised the importance of subcategorising CFS studies. [\[18\]](#)

In the light of current awareness of the overriding need for consideration of subgroups within CFS (including that which has emerged from Seattle), there is concern that if some of the content of chapter 3 of the present draft is incorporated into the final version, then the UK CMO's Report may be immediately dismissed and be held in derision by well-informed clinicians and patients alike.

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- [\[1\]](#) A Subgroup Analysis of Cognitive Behavioural Treatment Studies. Fred Friedberg. *JCFS* 1999;5:3-4:149-159
- [\[2\]](#) Estimating rates of chronic fatigue syndrome from a community-based sample: a pilot study. Jason LA et al. *Am J Community Psychol* 1995;23(4):557-568
- [\[3\]](#) Politics, Science and the Emergence of a New Disease. The case of Chronic Fatigue Syndrome. Jason LA et al. *Am Psychol* 1997;52:9:973-983
- [\[4\]](#) Chronic fatigue syndrome, Fibromyalgia and Multiple Chemical Sensitivities in a community-based sample of chronic fatigue syndrome - like symptoms. Jason LA et al. *Psychosom Med* 2000;62(5):655-663
- [\[5\]](#) Brain MRI abnormalities exist in a subset of patients with chronic fatigue syndrome. John DeLuca, Benjamin H Natelson et al. *J Neurol Sciences* 1999;171:3-7
- [\[6\]](#) Fatigue 2000 Conference Proceedings. The National ME Centre in conjunction with The Essex Neurosciences Unit. 23-25 April 1999
- [\[7\]](#) Severe and very severe patients with chronic fatigue syndrome: perceived outcome following an inpatient programme. DL Cox LJ Findley. *JCFS* 2000;7(3):33-47
- [\[8\]](#) Symptom patterns in long-duration chronic fatigue syndrome. Fred Friedberg et al. *J Psychosom Res* 2000;48:59-68
- [\[9\]](#) Editorial. Roberto Patarca-Montero. *JCFS* 2000;7(4):1
- [\[10\]](#) The Chronic Fatigue Syndrome: A Comprehensive Approach to its Definition and Study. Keiji Fukuda, Michael C Sharpe, Simon Wessely et al. *Ann Int Med* 1994;121:12:953-9
- [\[11\]](#) Conference Calls for Serious Research. T.Lupton. *CFIDS Chronicle* 2001;14:1:12-13
- [\[12\]](#) Directions in Immunotherapy. Roberto Patarca-Montero. *The CFS Research Review* 2001;2:1
- [\[13\]](#) Subtyping patients with Chronic Fatigue Syndrome in a Community Based Sample. Leonard A Jason et al. Presented at AACFS, January 2001 # 011
- [\[14\]](#) Cytokine Levels in CFS Patients with a Different Immunological Profile. Kenny De Meirleir et al. Presented at AACFS, January 2001 # 017
- [\[15\]](#) A Definition Based Analysis of Symptoms in a Large Cohort of Patients with Chronic Fatigue

Syndrome. Pascale De Becker et al. Presented at AACFS January 2001 # 019

[\[16\]](#) Use of Factor Analysis in Detecting Subgroups (of CFS patients). Paul H Levine et al  
Presented at AACFS January 2001 # 052

[\[17\]](#) Symptom Patterns of CFS in Adolescents. Katherine Rowe et al. AACFS Jan 2001 # 064

[\[18\]](#) A multicenter study of autoimmunity in CFS. K.Sugiura, D Buchwald, A Komaroff, P Levine,  
S Wessely, EM Tan et al. Presented at AACFS 2001 # 037