

What is CFS, and what is ME?



Peter White

Bergen, October 20th 2009

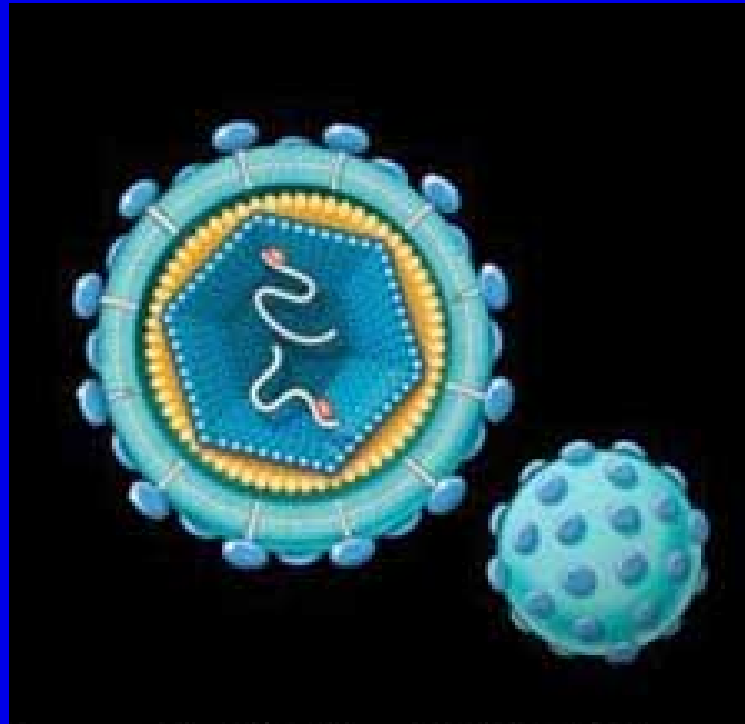
Agenda

What is CFS?

What is ME?

Define your phenotype.....

XMRV and CFS



Cross-section of XMRV provided by Robert H. Silverman, Ph.D., Lerner Research Institute, Cleveland Clinic, illustration by David Schumick, BS, CMI and Joseph Pangrace, BFA, CMI. Reprinted with the permission of the Cleveland Clinic Center for Medical Art & Photography © 2009. All Rights Reserved

THE SUNDAY TIMES 25 JANUARY 1987

Virus research doctors finally prove shirkers really are sick

by Neville Hodgkinson
Medical Correspondent*

It has also been called

A CHRONIC disease that

BOYD DISEASE

Proc. Natl. Acad. Sci. USA
Vol. 88, pp. 2922–2926, April 1991
Medical Sciences

Retroviral sequences related to human T-lymphotropic virus type II in patients with chronic fatigue immune dysfunction syndrome

(Epstein–Barr virus syndrome/infectious mononucleosis/myalgic encephalomyelitis/polymerase chain reaction/*in situ* hybridization)

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Postviral puzzle

ne investigations are geared to find these antibodies, and the fact that they do not always exist in sufferers from PFS has frustrated many a researcher.

However, some viruses seem to be more crafty. Although

New medical research should prove 100,000 'neurotic' people are genuinely ill. Report by
OLIVIA TIMBS

rather scathing about this test as proof positive of PFS. 'That is of little value,' he says 'because all it shows is that the person is infected by that virus. It sheds no light on the link between the infection and the symptoms. And why does it

me essential

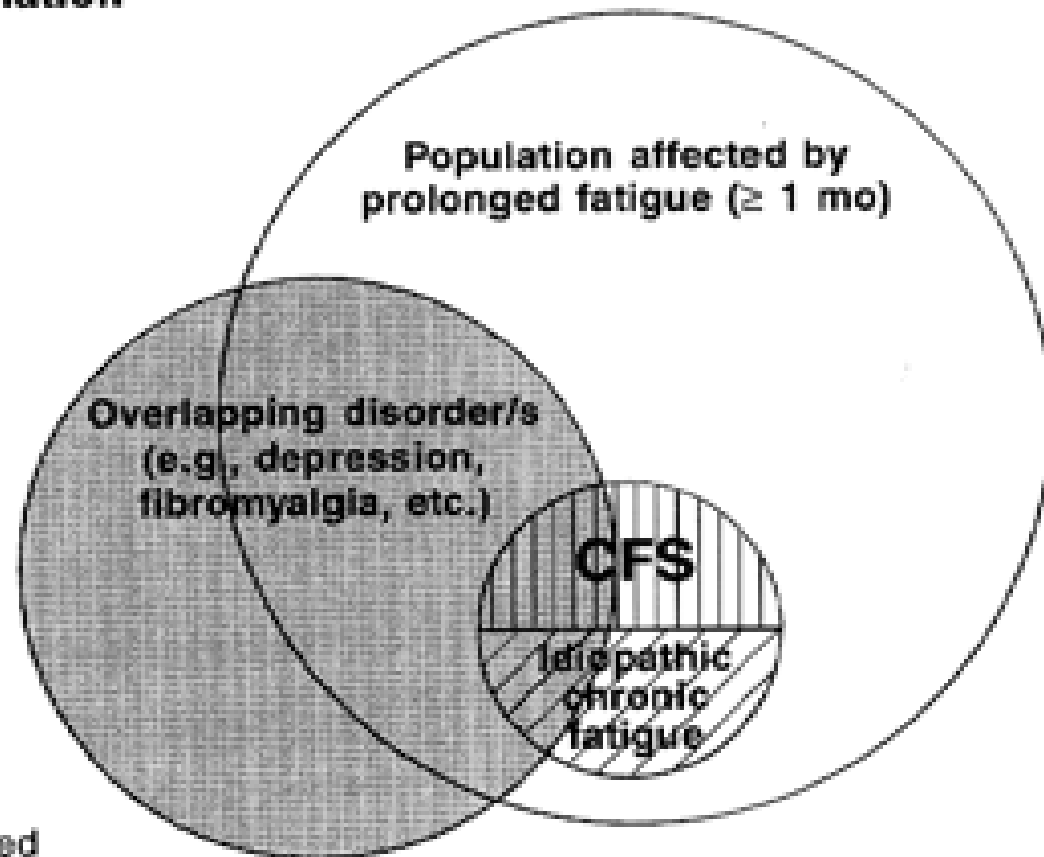
The magazine of The ME Association • Issue 100 • January 2008





How you define CFS will
determine what you find

The general population



Clinically evaluated
= unexplained
chronic fatigue

Does the ICD-10 help?

No -

At least six ways to classify CFS

Myalgic Encephalomyelitis

G93.3 in Neurology chapter of ICD-10

Postviral fatigue syndrome,

Includes:

benign myalgic encephalomyelitis

Chronic fatigue syndrome, postviral

Neurasthenia

F48 in ICD-10 mental disorders chapter

Neurasthenia

Excludes postviral fatigue syndrome

Includes fatigue syndrome

Other ways to classify CFS

F45.1 Undifferentiated somatoform disorder

F45.3 Somatoform autonomic dysfunction

Includes:

Da Costa syndrome,

Neurocirculatory asthenia

F45.9 Somatoform disorder, unspecified

Other ways to classify CFS

R53.82 Chronic fatigue, unspecified

Includes:

Chronic fatigue syndrome NOS

R54 Senile asthenia!

Can we use research criteria?

7 to choose from

7 research criteria

- CDC 1988
- Australian 1990
- Oxford 1991
- London ME 1993
- CDC revised 1994
- **CDC revised 2003**
- Brighton (post-vaccine) Collaboration, 2007

CDC (international) definition of CFS

- 6/12 of persistent/relapsing unexplained fatigue
- of new onset
- not the result of on-going exertion
- not substantially relieved by rest

CDC CFS

4 associated symptoms:

sore throat

tender lymph glands

myalgia

arthralgia

new headaches

unrefreshing sleep

post-exertion malaise

poor memory or concentration

CDC definition of CFS

- Substantial disability
- Medical and psychiatric exclusions

Recent audit of my clinic

- 250 new patients seen
- 54 (22%) - alternative psychiatric diagnosis
- 47 (19%) - alternative medical diagnosis

Risk of major depressive illness with chronic physical disorders

CFS	7.2
Fibromyalgia	3.4
Peptic ulcers	2.8
COPD	2.7
Migraine	2.6
Back pain	2.3
Cancer	2.3
MS	2.3

SB Patten et al, 2005 (n = 115,071)

No empirical support for CDC criteria

Swedish twin population study
(n = 31,000):

CFS-like illness; no CDC specificity
Sullivan et al, 2005, Kato et al, 2008

CDC population studies in USA:

For every patient with CDC CFS, 2-8
times more with disabling fatigue.

3 clinical criteria

- Canadian 2003
- RCPCH 2004
- NICE 2007

Canadian criteria for ME

- Fatigue
- Post-exertional fatigue/malaise
- Sleep dysfunction
- Pain

Any 2 of:

“confusion, impairment of concentration and short-term memory consolidation, **disorientation**, difficulty with information processing, categorizing and word retrieval, and perceptual and sensory disturbances – e.g. spatial instability and disorientation and inability to focus vision. **Ataxia**, muscle weakness and fasciculations are common. There may be overload phenomena: cognitive, sensory – e.g. photophobia and hypersensitivity to noise - and/or **emotional overload**, which may lead to “crash” periods and/or anxiety.”

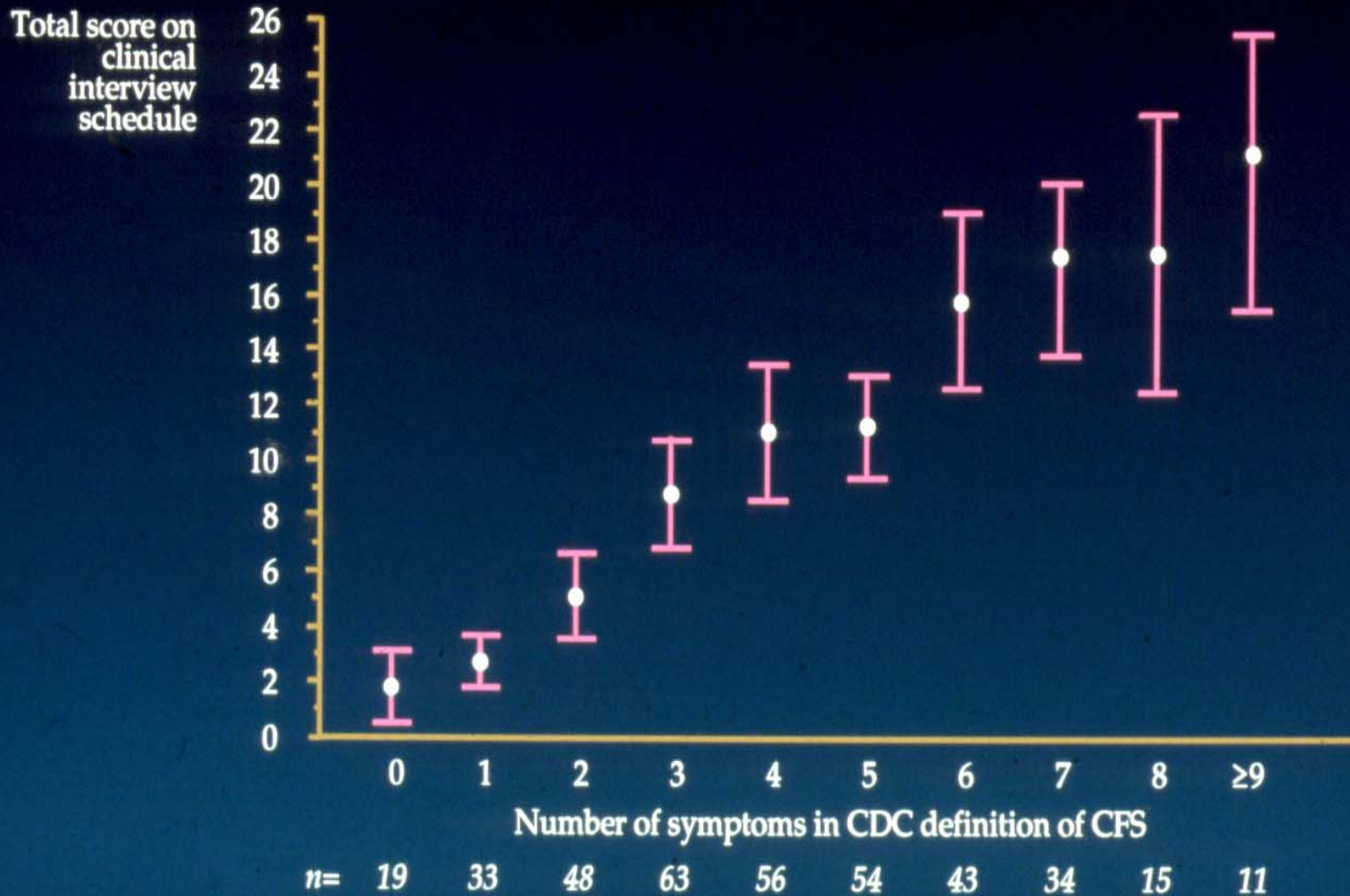
“At Least One Symptom from Two of the Following:

__ a. Autonomic Manifestations: orthostatic intolerance - neurally mediated hypotension (NMH), postural orthostatic tachycardia syndrome (POTS), delayed postural hypotension; light-headedness; extreme pallor; nausea and **irritable bowel syndrome**; urinary frequency and bladder dysfunction; palpitations with or without cardiac arrhythmias; exertional dyspnoea.

__ b. Neuroendocrine Manifestations: loss of thermostatic stability – subnormal body temperature and marked diurnal fluctuation, sweating episodes, recurrent feelings of feverishness and cold extremities; intolerance of extremes of heat and cold; marked weight change - anorexia or abnormal appetite; **loss of adaptability** and worsening of symptoms with stress.

__ c. Immune Manifestations: tender lymph nodes, recurrent sore throat, recurrent flulike symptoms, general malaise, new **sensitivities to food**, medications and/or chemicals.”

Psychiatric morbidity and CDC CFS symptoms



NICE

4 months of fatigue with:

- new or specific onset (not life long)
- persistent and/or recurrent
- unexplained
- substantial reduction in activity
- characterised by post-exertional malaise/fatigue

NICE 2

One of:

- The 8 CDC symptoms plus:
- general malaise or 'flu-like' symptoms
- dizziness and/or nausea
- palpitations in the absence of identified cardiac pathology
- Normal exclusions

CDC criteria give you reliability,
but not validity.

Always measure comorbid
conditions.

Is the CFS heterogeneous?



The measures, US style!

Medical and drug history

Hormones ++

Immune tests +

Polysomnography

Gene polymorphisms

Gene expression

Symptoms

Disability

IQ

Psychiatric exam

Analysis

- Principal components analysis (PCA)
- Latent Class Analysis (LCA)
- 121 chronically fatigued women
- 38 healthy matched controls

Vollmer-Conna U et al, 2006

Five endophenotypes

1. Obese & hypnoeic
2. Obese, hypnoeic & stressed
3. Insomnia & pain (myalgia)
4. Symptomatic, depressed
5. Symptomatic, depressed, insomnia, stressed and menopausal

External validation of endophenotypes

- 5 groups: demographic and clinical
- 3 groups; gene expression
- 3 groups: SNPs
- Replication in Georgian sample

Aslakson E et al, 2009

One functional somatic syndrome

CFS patients have close comorbidity with:

- Irritable bowel syndrome
- Fibromyalgia
- Regional pain disorders

Are they all part of the same disorder,
presenting to different specialists?

YES - Wessely and Sharpe, Lancet 1999

NO – Wessely and White, 2004

UK GPRD study

- 4,388 patients with CFS/ME/PVFS
- IBS and healthy matched controls
- Both ill groups - more premorbid mood and other functional disorders
- But triggering infections differentiated them.

Gallagher A et al, 2009

Common factors predispose to all
functional somatic syndromes

Uncommon triggers differentiate
functional somatic syndromes

What is ME?

- Myalgic encephalomyelitis
- First described in a 1956 Lancet editorial describing epidemics of fatigue with neurological symptoms and signs.

Royal Free hospital epidemic of 1955 (M Ramsay)

- 74% “showed objective evidence of involvement of the central nervous system”
- “heavy involvement of the cranial nerves”
 - “Objective evidence of brain stem and spinal cord involvement..”
 - “Paralysis of the face occurred in just under 20%..”

When did ME become endemic?

1978 conference - at the UK RSM

Epidemic “ME” became endemic

Organic incurable neurological disease

What message does this give our patients?

me essential

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The effect of a doctor's "ME" label on prognosis

- "ME" lasted longer than "CFS".
- "ME" patients had more consultations both in general and specifically for fatigue.
- No differences before diagnosis

Hamilton WT et al, 2005

Conclusions

- CFS exists, but is hard to define
- Make sure it's not something else
- Watch out for comorbid disorders
- Beware what you mean when you give a diagnosis