What is chronic fatigue syndrome; and what is ME?

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Bart’s and the London

Agenda

What is CFS?

- ICD-10
- Research criteria
- Clinical criteria
- One functional somatic syndrome versus heterogeneity

What is ME?

- Original epidemic ME
- Diagnostic labels affect prognosis

Is it physical or mental? It’s both

NEWEST MYSTERY ILLNESS:

CHRONIC FATIGUE SYNDROME

Mystery malaise

Once dismissed as the 'yuppie flu,' chronic fatigue syndrome is increasingly recognized as a debilitating disease that may afflict millions

M.E.

the mystery illness

Distressing symptoms usually inspire sympathy. Not so with myalgic encephalomyeli[tis]. Too often sufferers coping with physical fati[gue] them[selves]

YOUR BODY - YOUR ILL

Mysterious ME

M.E. the mystery ill.

IF YOUR DOCTOR THINKS IT'S ALL IN YOUR MIND... don't

assume you're just neurotic. You may be suffering from one of the 'new' illnesses that doctors are still having difficulty diagnosing

Does the ICD-10 help us?

No -

At least five 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!

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

No empirical support

- Population study of Swedish twins (31,000):

  CFS-like illness; no CDC specificity

  Sullivan et al, 2005, Kato et al…

- Population study of 1,468 pairs of 8-17 year olds

  CDC not delineated

  Fowler et al, 2005

- CDC population studies in Wichita & Georgia:

  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.”

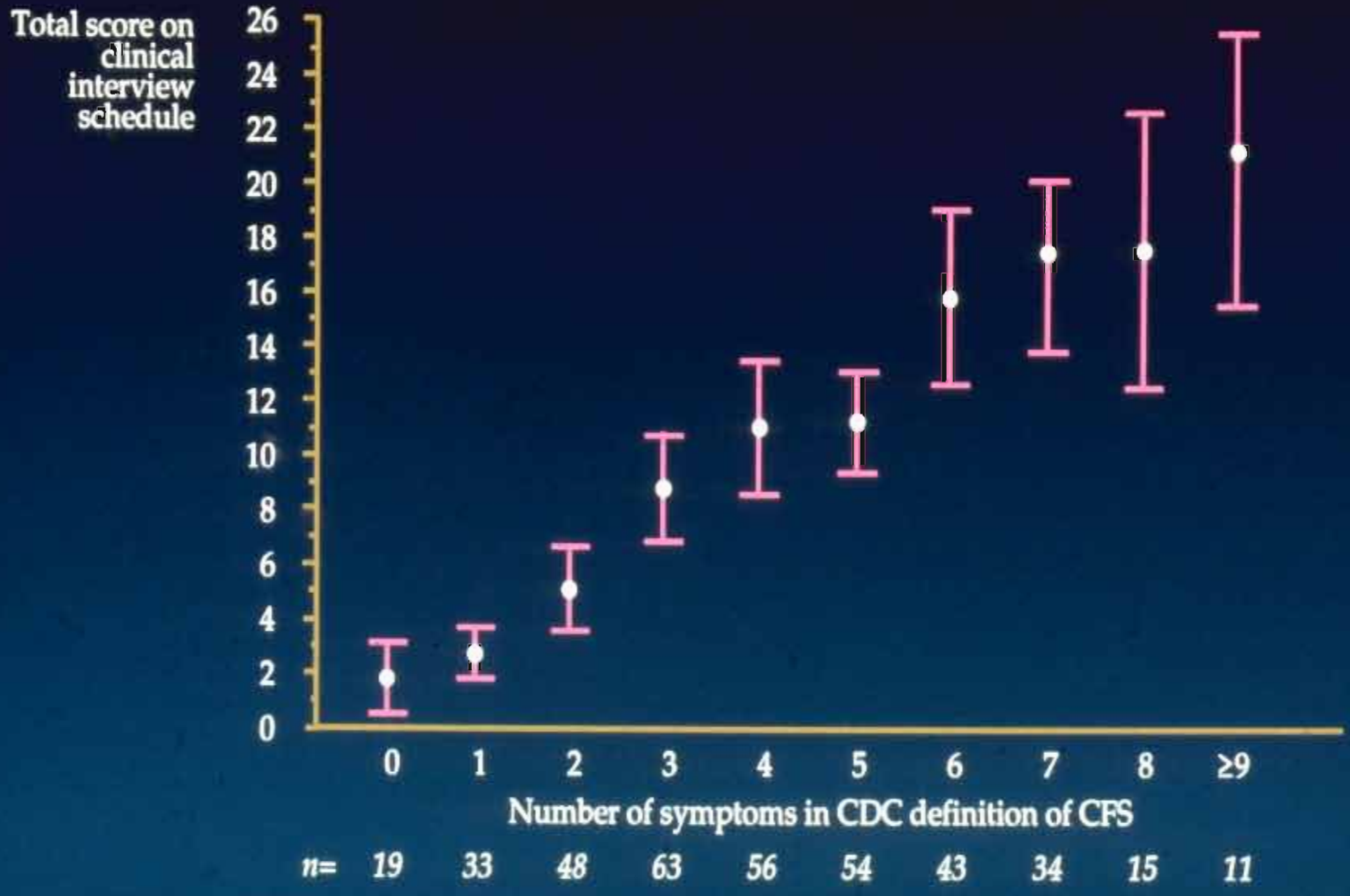
“At Least One Symptom from Two of the Following:

__ **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 dyspnea.

__ **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

RCPCH

- “..generalised fatigue causing significant impairment for 6/12 months for which no alternative explanation has been found...”
- “..the fatigue is likely to be associated with other ‘classical’ symptoms (..) such as difficulty in concentrating and disturbed sleep patterns and is classically exacerbated by effort (both mental and physical).”

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 – White, 2004

CFS studies with symptoms and demographics

- 744 clinic patients: 68% neurasthenia, 32% somatoform disorder

  Hickie et al, 1995 & 2001

All studies since have found heterogeneity

Is the CFS endophenotype heterogeneous?

Analysis

- Latent Class Analysis (LCA)
- 121 chronically fatigued women
- 38 healthy matched controls

Five ill sub-groups

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

Vollmer-Conna et al, 2006

External validation of groups

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

Should we give up the diagnosis of CFS/ME?

A working hypothesis:

CFS/ME may be the ***final common pathway*** from several different diseases with the same clinical presentation

It has utility, particularly for treatment

To lump or split?

- Population study of Swedish twins (31,000):

Two latent comorbid traits

1 dominated by mood disorders

2 all other disorders (FM, CFS, IBS, headaches)

"neither lumpers nor splitters are correct"

Kato et al (in press)

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 et al, submitted

What is ME?

- Myalgic encephalomyelitis
- First described in a 1956 Lancet editorial describing epidemics of fatigue with neurological symptoms and signs – the author later regretted doing this.

Royal Free epidemic of 1955 (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%..”

ME

- April 1978 conference - at the RSM!
- Organic incurable neurological disease
- What message does this give our patients?

me essential

The magazine of The ME Association · Issue 105 · January 2004

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

Conclusions

- CFS/ME exists, but is hard to define
- Broad based definitions are best
- Both heterogeneity and comorbidity should be addressed
- Beware what you mean when you give a diagnosis

Robert Kendell: “The distinction between mental and physical illness”

“Not only is the distinction between mental and physical illness ill-founded and incompatible with contemporary understanding of disease, it is also damaging to the long-term interests of patients themselves.”

BJ Psych 2001

Kendell again

"..if we do continue to refer to 'mental' and 'physical' illnesses we should preface both with 'so-called', to remind ourselves and our audience that these are archaic and deeply misleading terms."

BJ Psych 2001