More than just fatigue – a UK perspective

Julia Newton
Professor of Ageing and Medicine & Consultant Physician,
Fatigue Interest Group / Falls and Syncope Service
University of Newcastle
What is chronic fatigue?

- Fatigue and tiredness are not the same!
- Because there is little to see and no specific findings on examination or routine tests it is easy to dismiss it as psychologically based
- Good fun for cartoonists – but not much fun for patients
What is chronic fatigue?

'Typpie flu' may not be all in the mind - it might be in the genes

CFS/ME affects all social classes and all races but healthcare behaviour when ill biases social analysis limited to clinic referral!
What is CFS(ME)?

- Classified by WHO in ICD-10 as a neurological disorder G93.3
- Medical unexplained
  - Physiologically distinct from depression
  - Identifiable immunological, neurological, endocrine abnormalities that are consistent
- It is **not** a somatisation disorder
  - Somatisation may present as CFS and forms part of the differential diagnosis
  - Medically unexplained does not equal somatisation!!
What is CFS/ME?

- Severe debilitating fatigue causing interference with normal functions.
- Duration of at least 4 months
- No evidence for other medical or psychiatric problems.
- Typical history
- No pointers on examination to alternative diagnoses.
- Blood tests are normal
What is fatigue

- Fatigue is not the same as tiredness and is not relieved by sleep or rest.
- It is common to a broad range of chronic medical illnesses.
- Our understanding and recognition of the importance of fatigue in chronic illness is improving.
Fatigue

Also consider other organ-based disease (lung (COPD), heart, liver, kidney, bowel), malignancy and chemotherapy/radiotherapy, brain injury, PTSD, diabetes
What’s in a name?

CFS/ME form a spectrum with varying degrees of pain and fatigue; physiology is similar.
Epidemiology

- Prevalence of 0.2-0.4%
  - Average GP practice of 10,000 will have up to 40 patients

- Estimated annual prevalence 4000 cases/million population
Recognition of CFS/ME – in the UK

- Gradual acceptance of reality of the illness at official levels
  - 1996 - Kenneth Calman (CMO) commissioned report from Royal Colleges
  - 2002 – Report by Liam Donaldson (CMO)
    - CFS/ME Working Group. A report of the CFS/ME working group: report to the Chief Medical Officer of an independent working group. DH, 2002
  - 2005-6 DH funded specialist services for CFS/ME in England (but no funded services in Scotland or N. Ireland)
Is it a real illness?

- Medically unexplained = patient is mad or bad!
- Almost all patients are devastated by their illness and suffer depression as a result.
- Most will suffer severe hardship with loss of income, job, loss of hobbies, marital difficulties.
- Difficult to conceive that the majority of patients would wish to continue in this state
Is it a real illness?

- Scientific evidence now points to underlying physiological abnormalities.
- Psychiatric symptoms are secondary.
  - Anger
  - Frustration
  - Reactive depression and anxiety
Aetiology

- Uncertain
  - Two presentations:
    - Acute, usually following infective sounding illness
    - Gradual, no obvious predisposing factors
  - Unclear whether these are the same or separate illnesses
Infectious Agents

- Through 1960s disease attributed to chronic EBV (USA rules for benefits suggested patients must have high antibodies to EBV!!) ; other Herpes viruses (CMV)
- 1960s-1970s attributed to chronic Brucellosis
- 1990s suggestion of association with retrovirus HTLV-II (later refuted)
- 1990s association with Coxsackieviruses popular (based on poor quality test)
Infectious Agents

- 2009 – report from USA associating CFS/ME with murine endogenous retrovirus XMRV

- 2010 – 2011: findings not repeated. Original Lab confirms contamination
Aetiology

Genetic predisposition

Chronic fatigue syndrome

Intercurrent infection

Psychosocial background
Aetiology

- Evidence supporting an organic basis against a psychological basis
  - Neuronal abnormalities
  - Neurocognitive disorder
  - Autonomic dysfunction
  - Functional MRI scanning muscles
  - Genetic predisposition (multiple genes, immune system, brain); runs in families
  - Endocrine abnormalities (adrenocortical axis, sex hormones)
Genetic predisposition

Psychosocial background

Triggering event (infection)

Dysfunctional immunological response

Chronic cytokine abnormalities

Endocrine disturbance (adrenocortical axis)

Autonomic dysfunction

POTS, postural hypotension, abnormal muscle and skin blood flow

Mitochondrial abnormality?
Presentation

Chronic fatigue syndrome
- Unrefreshing sleep
- Headaches

Prolonged fatigue states
- Fatigue
- Pain
- Poor concentration
- Irritable mood

Depression
- Loss of motivation
- Loss of pleasure

Fibromyalgia
- Myalgia/arthralgia
- Tender points

Anxiety
- Panic attacks
- Avoidant behaviour

Irritable bowel syndrome
- Diarrhoea/constipation
- Abdominal pain
- Bloating
Typical symptoms

- Flu-like malaise
  - Worse after activity
- Muscle, joint pain, cramp
  - No joint swelling
  - Tenderness at FM points
- Disturbed body temperature
  - Inappropriate to environment
  - Inappropriate sweating

- Intolerances
  - Noise
  - Light
  - Touch
  - Smell
  - Medications
- Dizziness
  - Pre-syncope
  - Blackouts
  - Postural hypotension
Typical symptoms

- Palpitations
  - Anxiety
  - Postural
- Irritable bowel (100%!)
  - Bloating
  - Diarrhoea/constipation
  - Food intolerances (NOT allergy!!)
- Headache/migraine
- Tinnitus, vertigo
- Pins & needles
- Neurocognitive problems
  - Poor concentration
  - Poor short term memory
  - Word-finding difficulty
- Unrefreshing sleep
  - Sleep disturbance
  - Worse with over-exertion
- Sore throat/swollen glands
Diagnosis of CFS

- Diagnosis is primarily one of exclusion
- Diagnosis is therefore difficult and dependent on the skill of the clinician
  - Fatigue is not a unique symptom!
  - Fatigue is the final common pathway of many discrete diseases
  - Fatigue has a complex aetiology and involves multiple organ systems
  - Fatigue is NOT the same as tiredness
Chronic Fatigue Syndrome

- Exclusions to diagnosis of CFS (Fukuda)
  - Organ failure (emphysema, cardiac, liver, kidney)
  - Chronic infections
  - Rheumatic/chronic inflammatory conditions
  - Major neurological disease (MS, Myasthenia)
  - Systemic treatment for neoplasms
  - Untreated endocrine disorders
  - Primary sleep disorders (narcolepsy, sleep apnoea)
  - Obesity (BMI > 40)
  - Alcohol/substance abuse
  - Reversible causes of fatigue (operations, medication)
  - Psychiatric disorders (depression, bipolar disorder, psychosis, eating disorders)
Outcome of Clinical Assessment

- 2007 – 49% of patients referred from primary care do NOT have CFS/ME
- 2010 – Same figure, also replicated by CFS Service at St. Bartholomew’s Hospital, London
- Clinicians getting better at identifying other causes
- Earlier referral – other diseases may not yet have fully declared themselves
- Refer on to therapy teams for management where CFS/ME confirmed (CBT therapist, OT, Physio, Nurse)
Clinical Services

- Set up and funded by DH after CMOs report
  - Only for England and Wales
  - No services in Scotland
  - £8.5m investment
  - Requirement on PCTs to fund services (!)

- Regional Networks and Area Teams
  - Varying structures, pathways and models of care!
  - Varying effectiveness
Clinical Services

- NICE Guidelines introduced in August 2007
  - Recommendations for referral and management
  - Recommendations regarding appropriate and inappropriate treatments
  - Although these are ‘Guidelines’, clinicians are ‘expected’ to use them and PCTs are ‘expected’ to fund the services!
  - Recognised that “CFS/ME should be considered as disabling a condition as multiple sclerosis or rheumatoid arthritis”
Therapy Interventions

- Therapy interventions based around models used for chronic pain team (biopsychosocial model). Time limited.
- Combination of approaches from MDT
  - Activity-based
    - Pacing, graded exercise, avoidance of ‘boom-and-bust’
    - Sleep hygiene
    - General advice (diet, deconditioning, benefits, employment etc)
  - Lifestyle management
  - CBT; mindfulness; Lightning therapy
  - Physiotherapy & OT support
  - Individual and Group based
  - Use of drugs only for symptom management
Graded activity/pacing

- Do not give specific instructions ("walk x miles")
- Patient needs to understand the rules:
  - The correct activity level is the activity is the amount you can do today and then be able to do the same again tomorrow and the next day....
  - No boom-and-bust!
- Keep activity/symptom diaries – patient feedback
- Activity include mental AND physical activity
- Break tasks into manageable chunks with rest in between
- Increasing sleep disturbance = too much activity
Therapy Interventions

- No curative therapies (orthodox!)
  - Alternative sector offers many unproven therapies.
- Small Norwegian study reported significant improvement in small number of patients receiving rituximab (an anti-cancer drug)
  - This study needs to be repeated in blinded fashion with larger study group
- MRC Study did not show benefit from Pacing
Support in General Practice

- Manage pain:
  - Avoid opiates, NSAIDs (ineffective)
  - Use amitryptiline, valproate, gabapentin, duloxetine (small doses, slow increments)
- CBT – helpful (therapist must be familiar with CFS)
- Physical activity – physiotherapy ONLY if physio is familiar with CFS management
What are the outcomes?

- There is no curative therapy.
- NICE approved therapies are supportive not curative.
- Chance of spontaneous recovery is dependent on duration of illness.
- Early signs of improvement are a positive prognostic indicator.
- Lack of improvement by 2 years is a poor prognostic indicator.
How does CFS/ME affect patients?

- **Major issues are:**
  - Neurocognitive problems
  - Delayed response to activity (boom-and-bust)
- **Many patients will become:**
  - Agorophobic/social phobic (negative peer feedback (especially teenagers)
  - Trapped in negative feedback loop
  - Secondary depression/anxiety
  - Bed-bound = **disaster**!
    - Often due to complicity of family; secondary gain
Problems for patients with CFS/ME

- Lack of recognition of the illness
- Lack of empathy from healthcare professionals
- Discrimination
  - Medical
  - Employers/education
  - Friends and family
  - Benefits
  - Insurance
Conclusions

- CFS/ME is a chronic disabling disease with a genetic background, triggered by infection and with a link to psychosocial stressors
- There is increasing evidence of very specific physiological abnormalities that deny that the illness is just a psychological illness
- There are still no curative treatments
- Patients have major problems with disbelief within medical and benefits/insurance/pensions systems
Thank you for your attention