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**M.E.' WHAT DO WE KNOW?  
(real physical illness or all in the mind ?)**

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I am delighted to have the opportunity to address you all and I am most grateful for the University of Strathclyde and the Herald for hosting this series of lectures.

[opening slide]

I expect you know the joke about the expert - An expert is a person who comes from far away, has slides and has a book he wants to sell.

[Edinburgh slide]

Well I come from Edinburgh; which is of course a very long away. I have slides. And a book.

[Book slide]

In my lecture this evening, I would like to talk to you about myalgic encephalomyelitis ME also known as Chronic Fatigue Syndrome or CFS. Whilst this condition, which for convenience I will refer to as CFS, remains poorly understood and controversial, I shall argue that there are three important things we do know.

[Outline slide]

First, we know that CFS is real. Why people should ever think that it was 'not real' in itself is an interesting question, which I will address. What do we mean by real ? If real means a new illness the answer is - no its not. If real means a proven discrete biological entity - no its not. If real means a clinically convincing presentation with biological and psychological features the answer is yet it is. Definitely.

Second, we now know that in the majority of cases CFS can be effectively treated. That is we know how to reduce

disability and symptoms in the majority of cases. Although a large range of treatments has been tried, a Cognitive Behavioural form of treatment (sometimes referred to as CBT) has now been shown in randomised trials to have substantial benefits for patients with CFS. I will describe this treatment and the evidence for its effectiveness.

Finally we have a real illness that is associated with substantial suffering and disability. We have a relatively inexpensive treatment that can reduce suffering and disability in most patients. But few patients with CFS receive it - why? In seeking the reason for this we come back to our attitudes about what is a real illness. And I shall argue it is not just Tony Blair and Frank Dobson who are at fault but perversely patients themselves have played a part in denying themselves this type of treatment.

## **CFS IS REAL**

[slide person with CFS]

[Outline slide

What makes an illness real?

The first fact that I think is now generally, although perhaps not totally accepted about CFS is that it is 'real'. As someone who has been seeing patients with these symptoms for more than 10 years I have grown used to the question, "you see patients with ME don't - you - tell me - does it really exist?"

[Press slide ME all in the mind]

The issue of what makes an illness "real" is central to my talk tonight. As a controversial and high profile illness Chronic Fatigue Syndrome can teach us lessons about social and medical attitudes to illness in general and illness that is unexplained by pathological findings in particular.

Is CFS a new illness?

[Slide CFS - new illness]

The suffering and disability of patients with CFS may be real - but it is not new. Despite a lot of media comment referring for example to the 'ME generation' and much hypothesising relating CFS to modern concerns such as toxic exposures, there is very clear evidence that: a condition which appears to be identical was highly prevalent and caused similar concerns a hundred years ago.

[Slide Neurasthenia]

That condition was called Neurasthenia and the most prominent Clinician Researcher at the time was an American Neurologist called George Beard.

It is interesting to note that the causes of Neurasthenia - literally weak nerves, were thought to lie in the concerns of that time namely changing role of women, communication via the telegraph etc. In our time it is allergy and toxins.

Neurasthenia fell out of fashion in the early part of this century. This was probably partly because patients previously diagnosed as Neurasthenic was increasingly given the label of the psychiatric conditions of anxiety or depression. Not a popular alternative amongst many patients then either.

It seems likely however that over the following decades many patients continued to attend non-psychiatric physicians with similar symptoms and received a variety of other labels including Chronic Glandular Fever, Brucellosis and other hypothesised chronic medical afflictions. None of which are now considered likely explanations for the majority of cases.

[Slide names of Neurasthenia]

The modern history of CFS and ME has a number of strands.

[Slide ME]

There were epidemics most notably one in the Royal Free Hospital in 1995 for which the term myalgic encephalomyelitis or ME was coined in a leader in the Lancet.

The term ME subsequently "stuck" in the British literature.

In the United States, much Chronic Fatigue had been attributed to Epstein - Barr virus. The illness tended to be called chronic EBV infection.

However, by 1988 the evidence that EBV was not an adequate explanation for chronic medically unexplained fatigue became overwhelming. A working party met the Centres for Disease Control in the USA and created a new disease -- which they called Chronic Fatigue Syndrome.

Most researchers world wide now use the term Chronic Fatigue Syndrome because it makes no assumption as to the underlying pathology of the condition.

[Slide CFS definition]

Chronic Fatigue Syndrome is defined in the international definitions as follows:

The patient's main complaint is of fatigue.  
The fatigue causes a significant reduction in their activity and functioning.  
It has been there for a period of time - taken arbitrarily to be 6 months.  
Other symptoms are present eg muscle pains, poor concentration and others.

CFS is therefore not new in that it was well described at least a hundred years ago. Now have the benefit of a clear definition for cases however.

But concerns about reality of suffering impinge even on the name.

Some patients do not like the name because they believe it trivialises their condition - and it is too associated with psychological/psychiatric explanations. That it does not sound like a REAL illness.

A recent e-mail survey by a US patient organisation found that few if any patients wanted the name CFS to be used - most preferred Myalgic Encephalopathy ME - and there was a special plea for there to be no association with psychiatry!

Is CFS a unique illness?

[Slide - Is CFS a unique illness?]

Given that we now have a clear definition for CFS can we assume that, that clearly defines a distinct group of patients on whom to target research and treatment?

The answer to that seems to be that there is an increasing awareness amongst clinicians and researchers that there are many patients whose illnesses cannot be explained by conventionally defined disease pathology. These patients are not rare - in fact they make up the majority. The slide shows what proportion of patients' complaints in primary care are explained by disease...

[Slide from Kroenke]

In fact, it would seem that most medical specialities have at least one poorly unexplained syndrome. Whereas patients tend to present to infectious disease specialists with Chronic Fatigue often after an apparent viral infection, other medical specialists each have their own poorly understood presentation:

[Slide - unexplained syndromes]

For Neurologists it is probable headache, for Gastro-entérologists it is irritable bowel, for Rheumatologists it is fibromyalgia or fibrositis, for Dentists it is atypical facial pain, for Gynaecologists it is pre-menstrual syndrome and pelvic pain. Alternative medical practitioners are not immune and have their own syndrome of candidiasis and food allergy.

Furthermore a systematic review of these conditions by colleagues in London and me published in the Lancet suggests that these conditions are less distinct than they first appear to be. In fact the apparent differences seem to be at least partly because different specialists focus on symptom related to their bodily 'organ of interest' and show little interest in other symptoms. When one asks about other symptoms - they are in fact often present. There are now a number of publications commenting on the high rates of fibromyalgia, irritable

bowel, headache and other syndromes in patients identified as having CFS.

Furthermore there also similarities between these conditions in the associated factors such as sex distribution, in the evidence on aetiology and as far as we can tell in response to treatment.

We have to conclude therefore that the edges of what we call CFS are not sharply defined but it merges into a number of other common medically unexplained conditions. Of course it seems likely that Chronic Fatigue Syndromes as currently broadly defined will not be homogenous condition and in fact a number of attempts have already been made to sub-divide it. Again, there are various that believe that there is a core illnesses, which they may prefer to call ME. The existence of this remains to be seen however.

### **The problem of medically unexplained illness**

The problems of the patients with CFS in convincing others that their illness is new are therefore neither new nor unique.

Lets us Consider 3 patients: Mrs A, Mrs B and Mrs C, all 3 patients suffer from severe fatigue and exhaustion to the extent that they are not able to do their work. They each go to see their doctor and each receives a different diagnosis.

[Slide - 3 patients]

Mrs A receives a diagnosis of multiple sclerosis a chronic neurological condition, Mrs B receives a diagnosis of depression a chronic psychiatric condition and Mrs C receives a diagnosis of chronic fatigue syndrome, a chronic condition of uncertain status.

I would now like to ask you think for a moment which illness are the most real and what it is about the illness that makes it real.

The conventional wisdom is that illnesses are made real when they are legitimised by a doctor's diagnosis. Doctors makes a diagnosis based on finding objective abnormalities in the body. So, for Mrs A Magnetic Resonance Scan reveals brain lesions characteristic

of the condition. There is no doubt she has a real disabling illness.

For patients in whom no such pathological abnormality can be found it is conventional to regard the illness as not occurring in the body but in the 'mind'. Thus, patient B's depression is regarded as a "mental illness". Mental illness has different connotations from a physical illness. Patients with a mental illness are more likely to be regarded as weak to have something that is self-inflicted and to be being responsible for their own recovery. There is a sense that the illness is not as 'real' as the neurological condition.

The strength of these attitudes is attested to by the fact that they persist in the face of an increasing body of research demonstrating substantial perturbation of brain function, brain neurochemistry and endocrine function in the BODIES of people with depression.

Patient C who presents with predominately physical symptoms but who lack both pathological findings that would give her a medical diagnosis AND psychological symptoms such as depressed or anxious mood to locate them in the mental category are problematic. Which type of illness is it; mental or psychiatric? Does she have a legitimate physical illness or is it a doubtful mental illness.

### **Does CFS have biology?**

Yes - not conventional disease pathology - but biology. There is now evidence for a number of abnormalities in patients with Chronic Fatigue Syndrome. Some of these are replicated some are not. I shall focus on some of the more robust which are abnormalities in the brain in blood flow in neuro-transmitters and in the responsiveness of the associated hypothalamic pituitary adrenal axis. These findings are interesting because we focus our attention on the central nervous system. They are also similar to abnormalities in psychiatric conditions such as depression and anxiety disorders.

### *Brain scans*

These are abnormal - but similar to those of persons with depression

[Slide SPECT scans]

*Brain neurotransmitter*

Serotonergic system - different to depression but similar to other unexplained syndromes

[Slide-brain]

*Endocrine status - cortisol*

Low - like chronic anxiety

[Slide - endocrine system]

There are of course a long list of other controversial abnormal findings in Chronic Fatigue Syndrome including abnormal brain scans, immunology, autonomic reflexes, other hormone functions and even presence of chronic virus infection, though the role of none of these is clear at present.

### **Is there more than biology?**

*Patients beliefs*

The majority of patients with Chronic Fatigue Syndrome have no doubt how they prefer their conditions to be seen. Indeed the vehemence with which many patients insist that their illness is medical rather psychiatric basis has become one of the accepted hallmarks of the condition. Studies have found that it is one of the common features of CFS is the beliefs of the patient about the nature of their illness.

Patient's beliefs about the nature of CFS are important; they influence the reaction of other people including doctors; they may influence patient outcome and they may have an influence on treatment.

In fact there is strong evidence that how patients think about and cope with their condition has a major effect on the outcome. Patients who regard their illness as purely medical have a much worse outcome.

A systematic review of 26 follow up studies published by Joyce and other found that consistent predictors of poor outcome included patients beliefs about their illness.

[Slide Joyce et al]



The reason for this is not entirely clear but is most likely by the way they cope with the condition, a passive illness focused coping probably leads to a slower rate of recovery than an active problem solving style.

#### *Social context*

CFS also occurs in a social context. Clinically it is apparent that interpersonal stress particularly occupational stress appears to be a major factor giving rise to development of Chronic Fatigue Syndrome. It also seems that the disbelief of others including doctors and employers on the one hand

[Slide rejection by doctor]

And over-solicitousness and the reinforcement of unhelpful illness beliefs on the other can have an unhelpful effect on patients attitude and coping.

[Slide over caring]

Furthermore, the slow and difficult process of recovery is hampered by the presence of major obstacles such as the demand that one returns to a full-time stressful job.

[Slide demands of job]

CFS is then only adequately understood from a biological psychological and social perspective.

#### *In summary*

CFS is real it is definable. But it is not new or unique. It has biology - but it also has a psychology and sociology. It is this bio-psychosocial perspective that provides the basis for effective treatment.

## **2. CFS IS TREATABLE**

The second thing we do know about CFS is that certain treatments can be substantially beneficial to many patients.

[Slide - anti-fatigue pills]

### *Drugs*

Many drugs have been tried but few have proved to be useful.

There is some evidence for antidepressants and steroids. However neither have good trial evidence of long term benefit for all and there are potential hazards with steroids.

### *Non-drug treatments*

The main non-drug treatment is Cognitive Behavioural Therapy.

[Slide CBT]

The key ingredients of a cognitive behavioural approach to treatment are collaboration between patient and therapist. This means mutual trust and acceptance by the therapist of the reality of the patients suffering and disability and the willingness on behalf of both to consider social psychological and biological aspects of the condition.

Once collaboration is established, the patient and therapist will see each other regularly so that changes in the patient's behaviour can be discussed and planned. The patient then goes away to do "homework" experimenting with these changes and behaviour and comes back and tells the therapist of the results. Further experiments are then planned.

The initial strategies in such an approach are to improve the current level of coping with Symptoms and disability. The strategies used may involve normalising sleep; stabilising activity to a steady and manageable level and using strategies such as distract to manage symptoms.

The next step is for the patient to identify long term aims such as return to a sport or to work and short-term targets they would like to work towards. Patient and therapist thereafter plan small steps of increases in activity for the patient to attempt.

These increases in activity often run into difficulty. The reason may be partly because of biological intolerance of increased activity, partly because the patient fears making himself or herself worse and partly

because demands of others make it difficult to increase activity in the gradual way that is planned. The therapist works with the patient to discuss and manage these obstacles.

This approach has now been used in 3 published randomised trials and several others yet to be published. There are 2 British trials, which have used intensive Cognitive Behavioural Therapy, and both have found substantial benefits in patients functioning in symptoms. There is one Australian trial that used a brief form of a therapy, which did not find any substantial benefit over usual medical care.

[Slide of Oxford trial]

The first UK randomised trial was conducted by my own group when I worked in Oxford, and compared 16 sessions of individual CBT with usual medical care. As you will see there was a slow but substantial improvement in patient functioning such that 60% of patients had a good level of functioning at 12 months after entry compared with only 25% of those who received usual medical care.

Interestingly most of the improvement occurred after the end of the 16 sessions of treatment.

[Slides of Kings trial]

A second trial conducted by Simon Wessely's group in London, replicated the Oxford trial. It also addressed the issue of whether the treatment effect was a non-specific one of spending time with the patient by comparing CBT with time-matched relaxation therapy. This produced very similar findings to the Oxford trial.

Further as yet in published trials in the Netherlands and in other part of the UK have produced similar findings.

[Slide of exercise]

Why not just tell patients to do more. Studies of just gradual increases in activity more mixed results - it seems to help in selected patients but needs a psychological component.

So in conclusion we have evidence based safe and relatively inexpensive way of improving the function of patients with Chronic Fatigue Syndrome. It will come as no surprise to you to know that the similar reproaches of grade of activity in CBT have been shown helpful in a number of other medically unexplained syndromes.

### **3. BUT PATIENTS WITH CFS RARELY RECEIVE EFFECTIVE TREATMENT**

[Outline slide]

This leads me onto my final point which is the difficulty providing effective treatment for patients in the real world. The reality is, there is almost no availability of specialist Cognitive Behavioural therapy for patients with Chronic Fatigue Syndrome or any of the other related unexplained somatic syndromes in Scotland why.

The reason is of course due to NHS Priorities for use of resources. But given that the therapy is relatively cheap, it is also related to attitudes.

Purchasers and Health Care providers with hard pressed budgets are understandably reluctant to spend money on patients who are not going to die and for whom there is controversy about the "reality" of their condition. They are in this sense undeserving of treatment.

In my Opinion this is misguided and short sighted. The Personal and financial cost of a chronically disabling but largely treatable illness would far out way the Cost of providing treatment, however there is another problem.

The attitude of patients. Whilst individual patients are often accepting of indeed keen to seek such a treatment option, the groups representing patients the ME Action Campaign and the MB Association have hitherto taken a rather negative stance towards such treatment. For example let me show you what I found when I sought out the web-site of one of the patient groups.

[slide showing recommended treatment from Action for ME be....magnesium Injections and the nutritional supplement Efamol (a combination of evening Primrose oil and marine oil).]

As you will see they advocate only one or two treatments and these are certainly not CBT. In fact there are for treatments of which there is a far more flimsy evidence base.

This apparent reluctance by patients to accept Psychologically Sophisticated rehabilitative treatment serves to reinforce rather than challenge the reluctance of those who manage the budget to provide to spend on such treatments,

Fundamental to these views appear to be concerns about whether the illness is regarded as real or legitimate if it is seen as responding to a Psychologically Orientated treatment.

I would argue that such views although understandable are deeply mistaken.

## **CONCLUSION**

[Undeserving sick slides - only think they are ill]

In Summary, I was asked to talk to you about the illness called Chronic Fatigue Syndrome or Myalgic Encephalomyojiti<sup>5</sup>, Despite a large amount of research on this condition it remains Controversial and poorly understood, I have however argued that there is now a general acceptance amongst the majority of the clinical and research community that this illness is real but that it is not new and probably not unique.

Rather it overlaps with emerges into a very large group of patients who attend doctors with disabling distressing Symptoms for which conventional medicine finds no pathological explanation.

Our Society has difficulty with these illnesses because of our worldview, our metaphysics if you like. This is dualistic. Thus man was divided into a soul-less mortal machine capable of mechanistic explanation and manipulation. And a body-less soul, immortal, immaterial and properly subject to religious authority.

[Dualism slide]

The consequences are:

First, if a person's illness cannot be objectively seen it is only subjective and mental

If mental it is not real. Furthermore the person is either rational (and morally suspect for choosing to be ill) or irrational and blameless (but mad).

It seems that we have great difficulty thinking in a more holistic bio-psychosocial way about the suffering of a large proportion of the ill people in our society. Our limited dichotomous view is reflected in the bricks and mortar of the NEIS with its division into medicine and Surgery on the one hand and psychiatry and psychology on the other many persons being left in no-mans land in-between.

The history of CFS has its roots clearly in the last century. The issues surrounding it are shared with a number of other poorly understood or 'medically unexplained' illnesses.

Despite the age and size of this problem it seems that we have made little progress in achieving an understanding that permits effective treatment to be offered to and accepted by those affected.

Those who cannot be fit into a scheme of objective bodily illness yet refuse to be placed into and accept the stigma of mental illness remain to paraphrase Bernard Shaw the undeserving sick of our society and our health-service.

However things are changing. Neuroscience is breaking down the barrier between mind and brain. Doctor patient relationships are changing to give more credence to the patient's subjective experience. The collaborative integrative approach of good CBT provides one model of how we could proceed.

Perhaps we will do better in the next century. I hope so.