



***Journal
of
IiME***

***Invest in ME
International ME/CFS
Conference 2007 Special***

VOLUME 1 ISSUE 1



Welcome from Invest in ME

Welcome to the first Journal of Invest in ME – a combination of research, information, news, stories and other articles relating to myalgic encephalomyelitis (ME).

This first version is also serving a dual purpose in that it is acting as a component of the delegate's conference pack for the 2nd Invest in ME International ME/CFS Conference 2007, held in Westminster, London, UK.

Invest in ME welcomes delegates, presenters and media from ten countries around the world to the conference – emphasising that ME recognises no international boundaries. The interest in the conference also demonstrates the need for some of liME's main objectives – more education and proper funding for biomedical research into ME.

In this document we include articles from renowned ME experts who were not able to be present at the conference this year as well as those who are. We also include other ME experts who are presenting. liME hope to publish our journal throughout the year. As with the liME conference it will allow a platform for researchers, scientists, healthcare staff and politicians to be able to share and provide information relevant to those supporting, campaigning for or suffering from ME.

liME are firmly committed to raising ME awareness, facilitating education and lobbying for proper biomedical research into ME. We shall publish articles even though we may share different views – as long as an honest and transparent debate can occur.

However, one thing we shall never lose sight of is the tragedy of ME and the way it is treated - and so stories of real life with ME will be featured from people who are living with this illness on a daily basis, showing the tragedy, the courage and also the humour which people with ME and their families endure..

We hope our efforts and those of our regional and international contacts will ultimately avoid the need for all of our combined work and we can look forward to a treatment and cure for ME.

Welcome to liME. Welcome to London.

Disclaimer

The views expressed in this brochure by contributors do not necessarily represent those of Invest in ME. Patients with any illness are recommended to consult their personal physician at all times.

Facts About ME

An estimated 250,000 people suffer from ME in the UK

ME Story

I fell ill with the flu the same time as Antony, my then boyfriend/fiancé. He got over it, I didn't....

It was a struggle to get the illness recognized
- Wendy

Facts About liME

Invest in ME is made up of volunteers, ME sufferers and parents of children with ME

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Introduction – Professor Malcolm Hooper**Achievements, Hope, and Future Actions**

All three are brought together in this conference. We celebrate the successes of the last year in the high quality research studies that have consolidated the understanding of ME-CFS as a multi-system, multi-organ illness with an increasingly understood biological basis that offers a sound basis for challenging the spurious attempts to make ME an illness that is primarily psychogenic in origin - in contradiction to the established international system of nomenclature. A Quotable Quotes booklet available at the Conference illustrates this long and dishonourable conflict.

These achievements include advances in diagnosis and the increasing adoption of what are known as the Canadian Criteria/Guidelines. In truth these are North American Guidelines that involved co-operation between major clinical practitioners in both Canada and the USA. These should now be adopted as the international criteria and guidelines for the diagnosis of ME-CFS. The removal of the term CFS from any description of this illness would be a great advantage and provide clarity about both diagnosis and treatment. Much more is needed to define subgroups within ME-CFS with several useful schemes now available.

Scientific and clinical research has continued apace despite the reluctance of the MRC and Government in providing funding for such studies. Immunology has identified low NK, natural killer, cells as a key marker that could be adopted whilst the significance of oxidative stress provides another reliable marker in hsCRP, high sensitivity C-reactive protein. The importance of a diffuse inflammation associated with ME has been found in autopsy examinations of spinal cord and brain tissue and underlines the importance and accuracy of its designation as an inflammatory illness involving the central nervous system and new understandings of neurogenic pain also provides a mechanism for the severe pain experienced by many people with ME. The details of a common underlying mechanism continue to emerge involving PKR, protein kinase R, nitric oxide and intracellular responses to viruses, other micro-organisms, such as borrelia, rickettsia, chlamydia, leading to immune dysregulation. The role of chemicals and heavy metals are accommodated in these overarching and comprehensive mechanisms.

A very important new area of research concerns genetics which is beginning to address the complex issue of the interaction between genes and the environment and the questions of patient susceptibility to this and related overlapping syndromes. Hope for others is emerging from all these activities.

The scientific and clinical studies are identifying good tests to aid diagnosis and also new (and confirming some old) ways of treating this debilitating illness. Mitochondrial support linked to diagnostic tests is now available in one therapeutic regimen that many find helpful. Cytokines and their inhibitors may also provide effective treatment.

(continued on page 4)

Professor Malcolm Hooper (continued from page 3)

A catalogue of vested interests has been exposed which has given rise to the misleading judgements of the insurance industry and their advisors as well as the lack of the proper provision of appropriate benefits. The implications of the Inquiry for NICE and the MRC, who have become party to the machinations of the psychiatric lobby, are still being worked through.

An essential requirement for future progress is the need for all organisations concerned with ME-CFS to provide a coherent and unified approach to the illness and not to be distracted by the large sums of money being put into the current clinics that have been predicated on ME-CFS as a psychiatric illness. Together we shall succeed but divided we shall fail.

Finally there is the growing international collaboration that has now become apparent and provides grounds for rapid advancement in understanding ME. Canada, USA, Australia and New Zealand, and Norway have all made big strides forward. We have much to learn from each other and contribute to each others activities.

There is much to celebrate, there are real grounds for hope, and future effective actions can be recognised and agreed.

Invest in ME

Invest in ME (IiME) was formed by parents of children with ME and sufferers in September 2005 and registered as a UK charity in May 2006. The day to day running of the charity takes place in Hampshire and Norfolk.

IiME was formed to break with the established way of looking at ME. We are aiming to change positively the situation for people with ME and their families and carers. IiME has no paying members and no salaried staff – all of our work is voluntary.

During 2006 we established and strengthened regional and international contacts which we will develop in the future. Our campaigning for more informed education of doctors and for appropriate funding for biomedical research into ME has led to a busy year in which we have spoken with the Deputy Chief Medical Officer, the head of the MRC and numerous politicians.

As part of our campaigning we have responded to the proposed NICE guidelines which were, in our opinion, unfit for purpose; attended and given evidence to the Gibson report into M.E. which was published in November 2006; commented on the inadequate and misinformed NHS Plus Guidance leaflet and made representations to the Department of Work and Pensions on their guidance for M.E. and benefits.

The media have an important role to play in our efforts to raise awareness and change attitudes. To this end we have continued to build a good working relationship with many journalists, writers and broadcasters. This has been complemented by responding vigorously whenever possible to articles in the press.

During the last year we have attended the inquest of Sophia Mirza who died, "... **as a result of acute renal failure due to dehydration arising as a result of Chronic Fatigue Syndrome (M.E.)**". Her mother has lodged complaints with the GMC and the Social Services involved in Sophia's case and we will notify the outcome as soon as we can.

We are determined that what happened to Sophia must never be allowed to happen again.

Invest In ME will continue to campaign during 2007 and will build on the close working relationships we have with groups and clinicians around the world, as well as continuing to cooperate with ME Research UK in our joint endeavour to improve the lives of people with ME.

IiME LOGO

*What's in a logo?
The IiME Logo is based
on a double helix –
indicating our firm
commitment to treating
myalgic
encephalomyelitis as
the biological illness it is
and enforcing our view
that only biomedical
research will bring
about a cure for ME.*



Charity Nr: 1114035



The liME International ME/CFS Conference



The idea of an international conference began shortly after Professor Malcolm Hooper and Bruce Carruthers gave presentations at a meeting by ME Support Norfolk, in England at the start of 2005.

liME came into being in September 2005 and the need for similar presentations brought about the proposal to host a conference with more ME experts. liME decided London was the best place to hold the conference as it would allow easier access by politicians and prominent healthcare staff.

The first liME ME conference was held on ME Awareness Day, 12th May, 2006, with Professor Hooper, Dr. Bruce Carruthers, Dr. Byron Hyde, Dr. Jonathan Kerr, Jane Colby, and Professor Basant Puri and with Dr. Ian Gibson giving the key-note speech. The timing was prescient as Dr. Gibson would be soon embarking on his inquiry into ME by a group of parliamentarians – the Group for Scientific Research into ME (see later story).

Speakers and delegates from eight countries were present and the presentations from the conference subsequently appeared in the Journal of Clinical Pathology. Invest in ME's chairman was interviewed by the BBC and ITV and the conference was referred to in the New Scientist and several national newspapers.

The DVD of the conference was distributed to over twenty countries and is now sold as an educational DVD for healthcare and education professionals.

Those in ME Support Norfolk who initiated the presentations in 2005 and Professor Hooper planted a seed. From this grew the idea of the liME International ME/CFS Conference.

ME Story

I remember asking my doctor one day when I would stop feeling so tired!!! She said give it time - Robyn

Facts About ME

ME Research UK have a document (available also on the liME website) which has references to a multitude of research publications collected by Dr. J. Gordon Parish concerning possible ME epidemics.

The liME Conference – the Future

It is Invest in ME's intention to continue with the London conference until a treatment and cure is found for ME. This will be our way of raising awareness by providing a platform for researchers, healthcare staff, support, educational professionals, ME support groups and people with ME and the media, to enable the most relevant science, research, information and news to be heard.

The conference is now an annual event in May – ME Awareness Month. Invest in ME welcome the support of all ME groups, charities and individuals to make this an even better event next year.

We shall be working with our UK regional and international contacts to enable this and, even as we are organising the 2007 conference, we are looking ahead to the conference in May 2008.

Behavioral Interventions in ME/CFS. What a difference a decade makes!

Written for participants of the May 2007 UK ME Awareness Month events

By Dr Ellie Stein MD FRCP

As research progresses it becomes more clear that ME/CFS is heterogeneous group of biomedical disorders in which disabling fatigue, cognitive/neurological dysfunction, pain, autonomic dysfunction, immune dysfunction and gastrointestinal dysfunction are concurrently and chronically present. There is increasing evidence, much presented during the UK ME Awareness month, that ME/CFS is pathophysiologically distinct from other medical conditions and from psychiatric disorders.

In terms of the etiology of ME/CFS, the pendulum has swung from assumptions of infection as a primary linear precipitant in the 1950s to hypotheses of psychological/behavioral causation in the late 1980's to early 1990's. Now opinion is swinging back towards biomedical causes. But instead of a linear cause and effect, current research assumes the interaction of a group of facultative vulnerabilities (genetic, biochemical, environmental) with precipitants such as infection, environmental exposure or trauma to cause disease in a complex way which may differ in each individual.

Does behavioral medicine have a role to play in ME/CFS? Research suggests that the psyche plays a similar role in ME/CFS as in other biomedical conditions such as arthritis, heart disease and cancer. How one thinks about and reacts to one's illness does not in most cases change the underlying pathophysiology, but it certainly affects happiness, hopefulness and quality of life.

What is the evidence for this statement? A review of all published, controlled behavioral interventions in ME/CFS shows that there are subjective benefits in: fatigue, pain and health status. No other symptom groups have been reported upon. Neither cognitive function nor exercise tolerance seem affected by behavioral intervention. Furthermore, the subjective changes wane after 24 months (Edmonds *et al*, 2004; Price & Couper, 2000). These results are similar to those found in Fibromyalgia (Koullil *et al*, 2006).

Cognitive and exercise strategies are used in other disorders with similarities to ME/CFS such as Multiple Sclerosis and Rheumatoid Arthritis. In these conditions it is agreed that the role of behavioral intervention is symptom self management and psychological adaptation. Therefore using CBT/GET lacks controversy.

After more than a decade of debate, I posit that the ME/CFS community has moved beyond the bio-psycho debate. A close read of the methodology of the two most recent behavioral studies in ME/CFS show vastly expanded definitions of CBT and GET (Pardaens *et al*, 2006; O'Dowd *et al*, 2006). These studies bear little resemblance to the early studies which angered so many. The field has shifted significantly since the early 1990's.

Does behavioral medicine have a role to play in ME/CFS? Research suggests that the psyche plays a similar role in ME/CFS as in other biomedical conditions such as arthritis, heart disease and cancer. How one thinks about and reacts to one's illness does not in most cases change the underlying pathophysiology,

What is the next step in behavioral research in ME/CFS? Self Management is used in many chronic disorders especially arthritis, metabolic syndrome and pulmonary disease. The most common self management model world wide is the Stanford Model developed by Kate Lorig and others. This is a public health model in which lay patient experts facilitate groups for self referred persons with mixed disorders. The model has proven, positive, long term impact in disorders such as arthritis where evidence based medical care accessible to all participants. However in ME/CFS where many patients cannot find a disease literate physician, the Stanford model may not be as effective. Different adaptations of this model with more illness specific content are being studied in Australia and we are awaiting publications of that data.

Given that neither pharmacological nor behavioral interventions seems sufficient in ME/CFS, it is prudent to recommend integrated models in which biological, psychological and social factors are assessed and addressed.

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This requires:

- Increased funding for multidisciplinary ME/CFS research
- Understanding the pathophysiology of ME/CFS illnesses
- Defining distinct subgroups
- Educating health care professionals
- Ensuring integrated assessment and treatment is available to all persons with ME/CFS independent of financial means

References

References for this article may be obtained from Dr. Stein

Dr. Ellie Stein

Dr. Stein is a psychiatrist in private practice in Calgary, Canada [espc@shaw.ca]

ME Story

I attended the graded exercise programme 22 months ago. I was "sold" the programme under an amazing high degree of pressure and selling.

I could not do the increase of 30% of my activity, realistically though it was supposed to be 10%. The physio refused to believe that I could not do it! She told me I must be able to do it after I had tried and failed.

My entire immune system seemed to break down and since those few weeks I am now on high doses of anti viral medication from my GP and will be for years.

I would never do get/gat again or recommend anyone to do so. Try the pacing, but please refuse to do the Enforced targets. I was an innocent fool.

-M (UK person with ME)

Facts About ME

Due to relatively little funding given to biomedical research in the UK (compared to the extensive funding being given to psychiatric paradigms for therapies and trials) the amount of proper scientific research has been limited. However, there are over 4000 papers of biomedical research which contain indisputable facts related to the organic basis for ME.

More ME stories, including all of these contained in this brochure, are available at -

<http://www.investinme.org/mestorygallery1.htm>

Stories from parents of people with ME may be found at -

<http://www.investinme.org/mestorygallery2.htm>



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Professor Leonard Jason



Professor Leonard Jason
Professor of Clin. &
Community Psychology,
Director, Center for
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Dr. Leonard Jason, Ph.D., is among the most prolific of all CFIDS researchers. For more than a decade, Dr. Jason and his team at DePaul University's Centre for Community Research have worked to define the scope and impact of CFS/ME worldwide.

Professor Jason was intending to speak at our London conference but was forced to cancel due to other engagements.

Similar to other disorders such as cancer, it is likely that a number of distinct types of CFS exist, and that grouping all individuals who meet diagnostic criteria together is prohibiting the identification of these distinct biological markers of the individual subgroups

Exploratory Subgrouping in CFS: Infectious, Inflammatory, and Other

Karina M. Corradi, Leonard A. Jason,* Susan R. Torres-Harding

Keywords: chronic fatigue syndrome, subgrouping, physical disability, mental disability, psychiatric comorbidity

Introduction

Chronic fatigue syndrome (CFS) affects an estimated 836,000 adults in the United States (Jason et al., 1999), and is 3 to 5 times more common in women than men. CFS can impact any number of bodily systems including neurological, immunological, hormonal, gastrointestinal, and musculoskeletal (Friedberg & Jason, 1998). CFS is a diagnosis of exclusion. There are currently no specific diagnostic tests for its identification. Researchers have reported various biological abnormalities when investigating CFS, including hormonal abnormalities (Cannon et al., 1998; Moorkens, Berwaerts, Wynants & Abs, 2000), immune activation (Miller, Cohen & Ritchey, 2002), neuroendocrine changes, (Farrar, Locke & Kantrowitz, 1995) and neurological abnormalities (Cook, Lange, DeLuca & Natelson, 2001) among others. However, studies involving basic blood work appear to show no typical pattern of abnormality among individuals with CFS (Johnson, DeLuca & Natelson, 1999).

It has been suggested that a number of unique subgroups exist within the overall cluster of individuals diagnosed with this disorder (Cukor, Tiersky & Natelson, 2000; Jason et al. 2001; Johnson, DeLuca & Natelson, 1999). In the paper specifying the current US case definition for CFS diagnosis (Fukuda et al., 1994), the working group that developed the criteria referred to the importance of subgrouping within cohorts of individuals diagnosed with CFS. This demonstrates that, even as the current definitional criteria were being presented, there was an awareness of the heterogeneity within the identified group. After the publication of these criteria in 1994, many attempts to subgroup have been undertaken, but to date, no one method has proven to be consistently superior in differentiating subgroups.

Psychiatric comorbidity has often been considered a differentiating variable in research studies aimed at subgrouping (Borish et al., 1998; Cukor, Tiersky and Natelson, 2000; DeLuca, Johnson, Ellis & Natelson, 1997a; Masuda, Munemoto, Yamanaka, Takei & Tei, 2002). However, when Tiersky, Matheis, DeLuca, Lange, and Natelson (2003) examined individuals with CFS with and without psychiatric co-morbidity, they found that physical functional capacity was not worse in individuals with CFS and a concurrent psychiatric illness. Morriss and associates (1999) also found that depression was not associated with the reporting of pain, FM, IBS, or medically unexplained symptoms in individuals with CFS. Similarly, Ciccone, Busichio, Vickroy, and Natelson (2003) did not find that psychiatric illness, alone or in combination with a comorbid personality disorder, was associated with physical impairment.

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In contrast to the findings above, Borish, Schmaling, DiClementi, Streib, Negri, and Jones (1998) found evidence of low level inflammation, similar to that of allergies, in a subgroup of individuals with CFS. Borish et al. suggested that there might be two subgroups of individuals with CFS, those with immune activation (infectious or inflammatory) and those devoid of immune activation with other illness processes, including psychiatric disorders. Lutgendorf, Klimas, Antoni, Brickman, and Fletcher (1995) found that those patients with immune activation had the most severe cognitive deficits, while Natelson, Cohen, Brassloff and Lee (1993) found that those with ongoing inflammatory processes reported greater cognitive and mental disabilities. Buchwald, Wener, Pearlman, and Kith (1997) found individuals with CFS and chronic fatigue to have significant abnormalities in C-reactive protein (an indicator of acute inflammation) and neopterin (an indicator of immune system activation, malignant disease, and viral infections) when compared to controls. Buchwald et al. (1997) stated that groups of individuals with active low-level inflammatory, infectious processes could be identified and that this was evidence of an organic process in these patients with CFS. Cook, Lange, DeLuca, and Natelson (2001) found that individuals with an abnormal MRI and ongoing inflammatory processes had increased physical disability, suggesting an organic basis for some individuals with CFS. Conceivably, individuals without evidence of these infectious or inflammatory processes on basic laboratory screening tests might be more likely to contain individuals who had other neuroendocrine or neurologic illnesses that might not be readily identified using the minimum battery of laboratory of tests recommended by Fukuda and colleagues (1994) in order to diagnose CFS. However, those with infectious or inflammatory processes might be expected to be more physically impaired compared to those without these processes, based on research by Cook, Lange, DeLuca and Natelson (2001) and Lange, et al. (1999). There is also evidence that those individuals with CFS and with inflammatory processes report greater mental difficulties when compared to those individuals without them (Natelson, Cohen, Brassloff & Lee, 1993).

Clearly, individuals diagnosed with CFS are heterogeneous with varying illness course and disability patterns (Jason, Corradi, Torres-Harding, & Taylor, 2005). Similar to other disorders such as cancer, it is likely that a number of distinct types of CFS exist, and that grouping

all individuals who meet diagnostic criteria together is prohibiting the identification of these distinct biological markers of the individual subgroups. When specific subgroups are identified, even basic blood work may reveal a typical pattern of abnormality on diagnostic tests (DeLuca, Johnson, Ellis & Natelson, 1997b; Hickie et al. 1995; Jason et al., 2001).

This exploratory study considered several possible subgroups that fall under the umbrella diagnosis of CFS. It was expected that clinically significant groups would be found on the basis of abnormal blood tests. The laboratory tests that formed the basis for subgrouping were part of the battery of laboratory screening tests recommended by Fukuda et al. (1994). These groups consisted of an ongoing infectious group, an ongoing Inflammatory group, and an "Other" group (having neither infectious or inflammatory processes). Using these subgroups, this study sought to explore the relationships between membership in a subgroup, reported disability (both mental and physical), and psychiatric co-morbidity. It was hypothesized that the individuals with CFS would evidence higher levels of physical and mental disability than those in a control group, and that those in the Infectious and Inflammatory subgroup would exhibit higher levels of physical and mental disability when compared to the Other group. It was also hypothesized that the Inflammatory group would report greater mental difficulties when compared to the Infectious and Other groups.

Method

Procedure

Procedures developed by Kish (1965) were used to select one adult from each household contacted. The person with the most recent birthday was asked to complete the interview. A stratified random sample of several neighborhoods in Chicago was used, and a random sample of adults was screened. In stage one, 28,673 telephone numbers were contacted, with 18,675 adults completing the initial interview (see Jason et al., 1999 for further details). Persons who completed the initial screening stage of the study with indications that they may have had CFS, as well as a group negative for CFS (control group), were invited to participate in the second and third stages of the research study. Stage two involved administration of a structured psychiatric interview, the SCID, conducted by telephone. Stage three involved a

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Dr. Leonard Jason (continued)

medical exam at Mercy Hospital, including a physical exam, laboratory tests, including a complete blood count (CBC), white blood cell differential, antinuclear antibodies (ANA), sedimentation rate (Sed rate), rheumatoid arthritis (RA factor), chest X-ray, a detailed medical interview, and a structured medical questionnaire. Participants were also asked at this time to release previous medical records to the research study. The authors received IRB approval for conducting the study. Individuals who participated in the medical examination were provided financial compensation.

When each participant completed the study, a team of four physicians and a psychiatrist made the final diagnosis of CFS, Idiopathic Chronic Fatigue, Fatigue explained by a medical condition, or no fatigue. These physicians were familiar with the CFS diagnostic criteria and were blind to the experimental status of the participant. Two physicians independently rated each case to determine whether the participant met the CFS case definition (Fukuda et al., 1994). If a disagreement occurred, a third physician rater was used to arrive at a diagnostic consensus.

Participants

The participants for this project consisted of individuals with CFS and a control group. For the purposes of this study, it was important that the control sample include only individuals who presented themselves as mentally and physically healthy, due to the fact that abnormal medical test results were a primary variable. A total of 19 of 47 individuals in the control group were excluded from this study (e.g., on-going medical, sleep or severe and untreated psychiatric problems). The final sample included 31 in the CFS group (1 CFS participant was excluded due to lack of data on a critical variable), and 28 healthy controls. The CFS group consisted of 23 females and 8 males. The control group had 18 males and 10 females. Further demographic breakdown indicated that the CFS group had 5 African American, 14 Caucasian, 9 Latino, and 3 individuals who identified themselves as "other". The control group consisted of 4 African American, 20 Caucasian, 2 Latino, and 2 individuals who identified as "other".

Individuals with CFS were then sub-grouped into three groups according to medical evidence of possible inflammatory processes (as evidenced by abnormal eosinophils count, antinuclear antibodies [ANA], abnormal rheumatoid arthritis factor [RA factor], and abnormal sedimentation rate in the presence of one of

the prior mentioned inflammatory markers), medical evidence of possible current infection (as evidenced by abnormal results on lymphocytes count or sedimentation rate [Sed rate] without the presence of an inflammatory marker), and a group without evidence of either of these organic processes. Each of these medical markers is discussed in the measures section below. When subgrouped based on these criteria, 8 participants with CFS were categorized into the Other group, 8 in the Infectious group, and 15 in the Inflammatory group.

Measures

Measures used for this study included laboratory blood tests, a self-report of disability, and a structured clinical interview for the determination of psychiatric diagnosis.¹ [1All measures did not total 59 as all participants did not complete every measure.]

Standard laboratory tests were conducted during phase three of the full-scale study. Results used in the current study include: White blood cell (WBC) differential (specifically lymphocytes and eosinophils), rheumatoid arthritis factor (RA factor), antinuclear antibodies (ANA) and sedimentation rate (Sed rate). These laboratory tests were chosen for inclusion into the study based upon the recommendations of Fukuda and colleagues (1994) for diagnosing CFS. These tests are all part of the recommended minimum battery of laboratory screening tests suggested by this group in order to exclude other physiological causes of fatigue or another disease process. All blood-work completed for this study was analyzed through the laboratories at Mercy Hospital in Chicago Illinois, or National Health Laboratories Incorporated-Chicago, in Elmhurst, IL.

Eosinophils and Lymphocytes

Eosinophils and lymphocytes are specific types of leukocytes. To obtain the values presented and considered in this study, automated white blood cell differentials were performed. Differential white blood count is part of the complete blood count (CBC) and is composed of five types of leukocytes (WBCs whose chief function is to protect the body against microorganisms causing disease). These five consist of eosinophils, lymphocytes, neutrophils, basophils, and monocytes. The differential WBC is expressed in cubic millimeters and percent of total number of WBCs.

When elevated, eosinophil counts can indicate the presence of allergic inflammation, some forms of cancer,

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and parasitic disease. Significantly higher rates of allergy and allergic type reactions have been reported in the CFS population (Borish, et al., 1998). Several studies have also reported significant elevations of the eosinophil counts of individuals with CFS (Conti, Magrini, Priori, Valesini & Bonini, 1996; Baraniuk, Clauw, Yuta, Gaumont, Upadhyayula, Fujita, et al. 1998; Priori, Conti, Luan, Aprino & Valesini, 1994). The normal range endorsed by Mercy Hospital Laboratories for eosinophil count is 100-300 mL. This variable was coded as normal or abnormal depending on the test results from Mercy Hospital Laboratory.

When elevated levels of lymphocytes are found, this can be an indication of viral infection, chronic infection, and Hodgkin's disease, among others. Elevated lymphocytes have been reported in the CFS population (Patarca, 2001), and abnormal lymphocyte responses have also been noted (Krueger et al., 2001). However, elevated levels and abnormal responses have not been found in all studies (Brimacombe, Zhang, Lange & Natelson, 2002). The normal range endorsed by Mercy Hospital Laboratories for lymphocytes is 800-4400/mL. This variable was coded as normal or abnormal depending on the test results from Mercy Hospital Laboratory.

Rheumatoid Arthritis Factor (RA Factor)

RA factor measures antibodies in the serum of individuals with rheumatoid arthritis. When this test is abnormal, it indicates an inflammatory process such as rheumatoid arthritis, autoimmune disease and occasionally, infectious diseases. The presence of rheumatoid arthritis factor has been reported in the CFS population (Kerr et al., 2001). This laboratory test was conducted by National Health Laboratories Incorporated-Chicago, in Elmhurst, IL. Serum samples were first run undiluted, and if a positive result was found, the sample was then run diluted at a 1:10 dilution. The reference value for a normal result is < 1:20 titer. Ranges of 1:20-1:80 are positive for rheumatoid and other conditions. Results falling above 1:80 are positive for rheumatoid arthritis. Any positive results on this test were coded as abnormal. As Rheumatoid Arthritis is an exclusionary disorder for CFS diagnosis, all participants were screened for Rheumatoid Arthritis during their medical exam and this disorder was ruled out.

Sedimentation Rate (Sed Rate)

Sed rate measures the sinking velocity of blood cells, or

the degree of rapidity with which the red cells sink in a mass of drawn blood (Dirckx, 2001). Elevated Sed Rate can indicate bacterial infection, pelvic inflammatory disease, systemic lupus erythematosus, and red blood cell abnormalities (Kee, 2001). Abnormal sedimentation rates have been reported in CFS populations (Richards, Roberts, McGregor, Dunston & Butt, 2000). Results on this test are reported in millimeters per hour, and normal ranges depend on sex and age.

The Mercy laboratories normal range for males < 50 is 0-10.4 mm/hr, and for males > 50, 0-11.4 mm/hr. For females < 50 the normal range is 0-11.0 mm/hr and for females > 50, 0-20.0 mm/hr. This variable was coded as normal or abnormal depending on the test results from Mercy Hospital Laboratories.

Antinuclear Antibodies (ANA)

ANA tests for the presence of antinuclear antibodies in the blood. A normal result is negative. When positive, it is an indication of systemic lupus or other rheumatoid disorders, which are inflammatory diseases. Occasionally this test can be positive in the presence of specific types of infections. Elevated rates of ANA have been reported in the CFS population (Nesher, Margalit & Ashkenazi, 2001). Several reports of a specific type of ANA found in some individuals with CFS have been published (Itoh et al., 2000; Nishikai, et al., 2001).

Psychiatric Diagnosis

To measure current and lifetime psychiatric diagnosis, the Structured Clinical Interview for the DSM (SCID; First, Spitzer, Gibbon & Williams, 1995) was used. Previous studies have indicated that the SCID is a reliable measure of psychiatric diagnosis in the CFS population (Taylor & Jason, 1998). The SCID requires administration by master's level clinicians. To create the categories used in this study, all diagnoses identified as anxiety disorders by the DSM (such as generalized anxiety disorder, phobias etc.) were grouped together into one Anxiety Diagnosis variable, all disorders identified as depressive disorders (such as major depressive disorder, seasonal affective disorder, bipolar disorder etc.) into one Depressive Disorder variable, and all other psychiatric diagnoses (such as substance abuse disorders, somatization etc.) were grouped into an Other Psychiatric Diagnosis variable.

Disability

To determine disability level, the SF-36 (Stewart, Hays &

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Dr. Leonard Jason (continued)

Ware, 1988) was completed by all participants. The SF-36 is a 36-item questionnaire that assesses individuals' self-report on physical and emotional health currently, in the past four weeks, and compared to the same time last year. The SF-36 has eight subscales, and one reported health transition score. Two composite scores are available for the SF-36, the Physical Component Summary (PCS) and the Mental Component Summary (MCS). Internal consistency coefficients range from .89-.94 for the PCS, and .84-.91 for the MCS across age, gender, race, education, medical diagnosis, and disease severity. The current study used these summary scales to determine differences in physical health, and mental health (Ware, Kosinski & Keller, 1994).

Results

Initial analyses were conducted to determine if any significant differences existed between the control and the entire CFS group on sociodemographic variables. There was only one significant difference, which occurred for gender. Therefore, gender was run as a covariate in all subsequent analyses.

Subgroup Differences for Physical and Mental Disability

To consider the relationship between subgroup membership and reported physical disability, an ANCOVA was run with subgroup as the independent variable, PCS as the dependent variable, and gender as a covariate. Analyses indicated that significant differences could be found between the subgroups on the PCS ($p < .01$). Least Significant Difference post hoc analyses indicated that all three CFS subgroups reported significantly higher levels of physical disability than the Control group ($M = 56.1$). The Other group reported significantly higher levels of physical disability when compared to the Inflammatory group ($M_s = 29.2$ vs 39.2 , respectively), but it was not significantly different from the Infectious ($M = 34.7$) group.

Next, an ANCOVA was conducted with a subgroup as the independent variable, MCS (a measure of mental disability) as the dependent variable, and gender as the covariate. Analyses indicated that significant differences did exist between the subgroups for the MCS variable ($p < .01$). Following the significant omnibus test, post hoc analyses indicated that the Inflammatory group had significantly greater mental disability compared to the control group ($M_s = 36.5$ vs 50.8 , respectively), but was not significantly different from the Other ($M = 43.6$) or Infectious ($M = 39.7$) groups.

Relationships between Subgroups and Psychiatric Diagnoses

To attempt to understand the relationships that might

exist between subgroups and psychiatric diagnoses, logistic regressions were conducted considering subgroups as the independent variables (e.g., Other, Infectious, Inflammatory, and Control) and one psychiatric diagnosis per logistic regression (with the following dependent variables in separate analyses: current depression, current anxiety, and current other psychiatric diagnosis).

No significant differences were found among the subgroups and the presence of depression, anxiety disorder, or other psychiatric diagnosis.

Because prior studies have indicated that the CFS groups have significantly higher rates of current and lifetime psychiatric co morbidity, the analyses above were performed on current and any lifetime psychiatric diagnoses.

Two logistic regressions used current psychiatric diagnosis and lifetime psychiatric diagnosis as dependent variables. The odds that an individual in the Infectious group also had a current psychiatric diagnosis were 6.13 times higher when compared to individuals in the control group. The odds that individuals in the inflammatory group had a current psychiatric diagnosis were 12.65 times higher when compared to control group members.

The second logistic regression considered lifetime psychiatric diagnosis of any kind between membership in one of the subgroups, and membership in the control group. Analyses indicated that the odds that individuals in the inflammatory group had a psychiatric diagnosis at some time in their lives were 18.66 times higher when compared to individuals in the control group.

Ethnic Differences

Prior to sub grouping, no significant differences existed between the control and CFS groups on ethnicity. However, when examining the three subgroups separately with the control group, chi square analysis indicated that significant differences did exist between the four groups [χ^2 (3, $N = 59$) = 10.00, $p = .019$]. The Infectious group (91% minority, 9% Caucasian) were significantly more likely to be of minority status than the Other (32% minority, 67% Caucasian) and control (37% minority, 63% Caucasian) groups, but they were not significantly different from the Inflammatory (56% minority, **44% Caucasian**) group.

(continued page13)

Dr. Leonard Jason (continued)

Discussion

While it was hypothesized that the Infectious and Inflammatory groups would be significantly more physically impaired compared to the Other group, we found that the Other group reported significantly greater physical impairment compared to the Inflammatory group. In the present study, the Other group might have reported greater physical impairment because of other on-going physiological processes.

For example, supplemental analyses indicated that the Other group was significantly more likely than the Infectious group to present with symptoms of orthostatic intolerance, specifically, dizziness immediately following standing, and dizziness when turning the head. The Other group might have contained individuals with ongoing illness processes that were not identifiable by the laboratory tests available for this study. Orthostatic intolerance is best diagnosed using tilt-table testing, which was beyond the scope of the current study.

The Inflammatory group was significantly different only from the control group. This result is consistent with past findings of greater mental disability in the Inflammatory group when compared to the control group, and is consistent with past research indicating individuals with ongoing inflammatory processes are more likely to report greater mental difficulties (Natelson, Cohen, Brassloff & Lee, 1993).

When measuring participants' psychological status, the Other group was the only chronic fatigue subgroup that did not have significantly elevated psychiatric diagnoses. No significant relationships emerged between membership in the Infectious, Inflammatory, and Other groups, and current diagnosis of depression, anxiety, and any other psychiatric diagnosis. However, when examining simply the presence or absence of any current or lifetime psychiatric disorder, the Inflammatory group was more likely to have a current or lifetime psychiatric diagnosis when compared to controls. Also, individuals in the Infectious group were found to be more likely to have a current psychiatric diagnosis when compared to controls.

It is possible that the presence of a chronic illness may put enough psychological strain on an individual that this strain contributes to or caused psychiatric diagnosis, or that the same processes that increase an individual's likelihood of

having a mental disability when inflammatory processes are present, may increase the likelihood of a psychiatric diagnosis.

It is also possible that the psychiatric symptoms are completely unrelated to the CFS diagnosis (Abbey, 1996).

The relationship between psychiatric diagnosis and CFS diagnosis is one that is far from being understood and therefore is much in need of further study.

Finally, the Infectious group had a greater number of minorities compared to other subgroups and the control group. It is well documented that minority and low SES populations are less likely to have access to health care (Richman, Flaherty & Rospenda, 1994). Language barriers, past experiences with the healthcare system, and different medical and religious beliefs may all contribute to minority participants being less likely to utilize health care, even if they have the access (Borrayo & Jenkins, 2003; Johnson et al., 1995). It is also possible that minorities who are immigrants are more likely to travel to their country of origin and be exposed to different infectious agents in their travels. In addition to this, minority participants may be more likely to be employed in hazardous or environmentally stressful occupations with exposure to infectious agents.

It is possible then that minorities in the present study had poorer health care utilization, and therefore were less likely to have had infectious processes treated.

The current exploratory investigation had several limitations. First, the medical tests used as the basis of subgrouping in this study were not exclusive indicators of infection or inflammation. Further, the distinction between infection or inflammation is often one that cannot clearly be made, as these two processes frequently occur together. While inflammation generally accompanies infection, there are distinct instances when inflammation occurs in the absence of known infection, such as allergic inflammation, or sub-clinical level rheumatoid arthritis. Future studies should seek to determine if clear differentiation can be made, with more accurate tests, between infection and inflammation. Second, the limited sample size for African American, Latino, Asian, and other minority groups necessitated the grouping of all minority participants into one larger minority group. It is difficult to be certain if the relationships found (i.e. that of minority participants being more likely to present with on-going infectious processes) are more likely in individuals who

(continued page 14)

Dr. Leonard Jason (continued)

have minority status in general, or if differences in findings are due to a specific minority group.

The current study had small sample sizes, and this could contribute to instability of results, limited generalizability and lack of statistical power.

Logistic regressions with small sample sizes can over-fit models and generate high odds ratios. Future research should consider larger sample sizes of each minority group to explore within-group and between-group differences.

It is notable that these findings emerged when forming subgroups utilizing only a basic battery of laboratory screening tests. These laboratory tests were conducted primarily for the purpose of screening out other major illnesses that might explain a person's chronic fatigue, as recommended by Fukuda and colleagues (1994). Many people with CFS exhibit only minimal or subtle abnormalities on these tests, and these abnormalities often are inconclusive or may not be acknowledged by the primary care physician because they do not lead to a diagnosis of another, more recognized disease process. Further, the more commonly reported physiological abnormalities reported in people with CFS, such as the presence of RNase L (Suhadolnik et al., 1997), adrenal insufficiency with subsequent low cortisol levels (Addington, 2000), the presence of orthostatic intolerance (Schondorf, Benoit, Wein, & Phaneuf, 1999), and immunological abnormalities (Patarca-Montero, Mark, Fletcher, & Klimas, 2000), can only be assessed using highly specialized, expensive, or experimental tests to which people with CFS and their physicians typically have little access.

This study demonstrates that subgrouping is possible using laboratory tests that are readily available and can easily be ordered by primary care physicians.

The identification of clinically significant subgroups is the logical next step in furthering CFS research. There might be multiple pathways leading to the cause and maintenance of the neurobiologic dysregulations and other symptoms experienced by individuals with CFS. Depending upon the individual and subtype, these may include unique biological, genetic, neurological, psychological, and socioenvironmental contributions. Previous research examining people with CFS as a homogenous group may have missed real differences that might exist among subgroups of people diagnosed with this illness.

Subgrouping might be the key to understanding how CFS begins, how it is maintained, how medical and

psychological variables influence its course, and in the best case, how it can be prevented, treated, and cured (Jason et al., 2005).

Acknowledgements & references

Request for these and reprints should be addressed to Leonard Jason, Center for Community Research, DePaul University, 990 W. Fullerton Avenue, Chicago, IL 60614.

ME Story

I was assessed for one ME clinic but they said I was too disabled and that there were other issues that needed to be worked on. They also said that because I was confined to a wheelchair they thought that would be too upsetting for the other members of their group
- Gary

ME Story

3 yrs ago I came down with what I thought was the flu, but I never recovered. After many doctors I was diagnosed with ME.

At this time last year I was able to still care for my own needs but as the summer progressed so did my illness. My ability to get up by myself declined. I had to have help getting to the recliner in the living room and to the bathroom. I started having problems feeding myself, my hands would shake so bad that the food and my drink ending up all over myself.

Then it got to the point that walking was impossible. I had a bedside commode that I used and my husband would carry me to the recliner.

In Nov it was decided that my mom would move in with us to help care for me. By that time I was totally bedridden unable to care for myself. - Blaze

INVEST in ME CAMPAIGNING for ME AWARENESS

ME AWARENESS MONTH

ME Awareness has traditionally consisted of a week in May – with 12th May being recognized as ME Awareness Day.

liME have been suggesting that only a ME Awareness Month is sufficient to mark the seriousness of this illness, with 12th May being recognized as the focal point of the month.

We are happy to join with ME Research UK to promote ME Awareness Month – a chance for people around the world to highlight the issues surrounding ME, to recognize the devotion of many carers and the courage of many sufferers of ME. It will also give more opportunity for serious discussion of research and enable ME to be seen more as a mainstream illness.



HAVE a CUPPA for ME



Although liME and other ME support groups are campaigning for ring-fenced funding for biomedical research into ME we also recognize that we need to help raise money via a voluntary donation effort. In late 2005 Invest in ME launched the **Have a Cuppa for ME** event. A simple idea to hold tea or coffee mornings with friends, relatives and neighbours.

Around the country groups have organised HACFME events and raised thousands of pounds which has gone towards biomedical research to charities such as ME Research UK.

More details can be found on the liME site – www.haveacuppaforme.org.



ME as a Notifiable Illness

Invest in ME are happy to work with other groups and charities for the benefit of people with ME and to make progress regarding the urgent issues which need to be tackled. Our recent campaign to have ME recognised as a notifiable illness in schools was made from an idea by Jane Colby. Jane is a former head teacher who has ME and who formed Tymes Trust. It is now ten years since Jane and Betty Dowsett made the report on ME. These studies along with those of Dr Nigel Speight have clearly shown that ME-CFS is a major illness responsible for most school absenteeism.

Our campaign called on the Chief Medical officer to make ME a notifiable illness in schools. With no government funding being directed at biomedical research we need as much data as possible in order to apply necessary diagnostics to this illness. By making ME a notifiable illness it would be possible to collate more exact figures for occurrence and geography of the illness. It would have a further advantage in ensuring that children's lives are not irreversibly disadvantaged due to lack of awareness. If the demographics were better understood Health and Education Authorities could better target their limited resources for the benefit of these sick children.

More on this may be found at –

<http://tinyurl.com/ypnv2q>

Dr Vance Spence & Dr Neil Abbot

ME/CFS: a research and clinical conundrum

This presentation was given at the ME research UK Colloquium in 2003.

My role is to provide an overview of the difficulties surrounding the illness, especially for those of you who are coming fresh to the topic from other scientific areas and specialties. One of our aims is to bring together experts from a variety of disciplines, some with little or no experience of ME/CFS, as we attempt to energise research into this condition with new ideas and novel approaches to solving its inherent problems.

The most widely-used definition of "Chronic Fatigue Syndrome" is that developed in 1994 by a consensus conference: the CDC-1994 (Fukuda et al., 1994) definition. This was developed in response to criticisms that previous definitions (including the CDC-1988) were too restrictive. It requires the presence of chronic fatigue of six months duration which is persistent or relapsing, of new or definite onset, not substantially alleviated by rest, not the result of ongoing exertion, resulting in a substantial reduction in activities, and leading to substantial functional impairment.

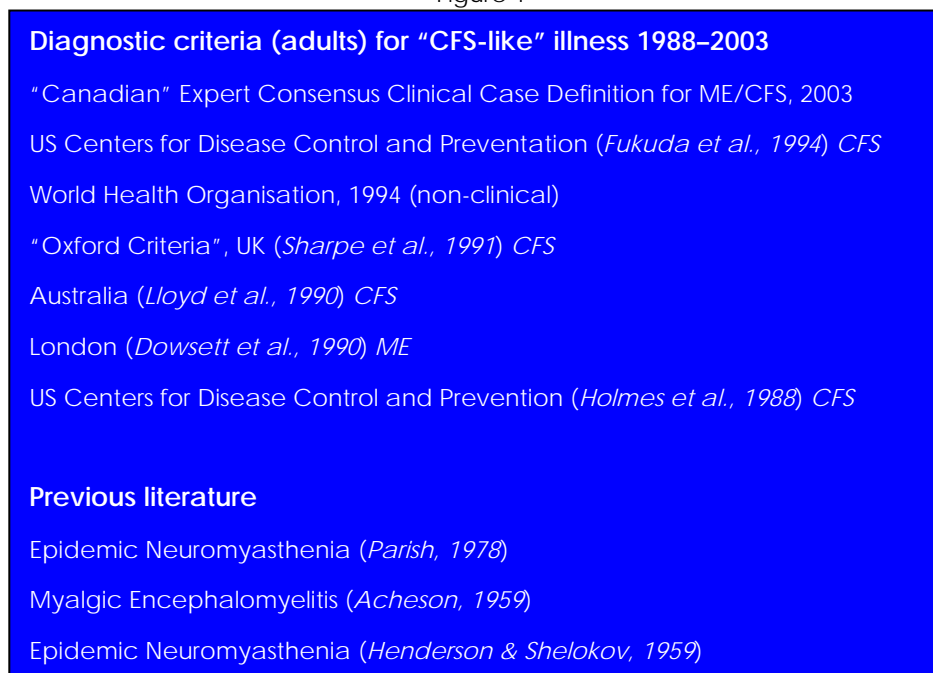
In addition, at least four of the following are required: sore throat, cognitive symptoms, tender lymph nodes, muscle pain, multi-joint pain, headaches, unrefreshing

sleep and post-exertional malaise. Cognitive or neuropsychiatric symptoms may be present, but the definition excludes clinically important medical conditions such as melancholic depression, substance abuse, bipolar disorder, psychosis and eating disorders. Some would argue that I could just mention this definition and sit down again; but in fact it is part of the problem, and it is worth examining why that is so.

As you can see, the definition relies on "fatigue" as its major criterion. For that reason many patients who fall under this diagnostic label hate the name — they call it the F-word — since for many of them "fatigue" per se is not the major problem, and does not best represent how they would explain their condition. Thus, this CDC-1994 definition is now widely recognised to have a number of limitations. These include the fact that symptoms are mainly self-reported (e.g. the clinical signs required in the CDC-1988 definition have been removed); the terminological criteria are vague (e.g., "fatigue", "malaise", "unrefreshing sleep", etc.); the specificity of the definition is poor, allowing heterogeneous groups of patients (e.g., those with somatoform disorders, fibromyalgia syndrome, etc.) to coexist under the one umbrella term (Salit, 1996; Jason et al., 1999); and it makes no attempt to differentiate

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Figure 1



ME/CFS: a research and clinical conundrum (continued)

patients on the basis of severity of illness or level of functional disability. Indeed, there is a growing realisation that the current CDC-1994-defined "CFS" term is an impossibly inclusive diagnostic construct, begging Simon Loblay (1995) to ask the ontological question: "Is CFS a recognisable disease entity with a unique pathophysiology, or is it a ragbag of common non-specific symptoms with many causes, mistakenly labelled as a syndrome?"

As an example, our work in Dundee has compared three groups of patients each fulfilling the CDC-1994 criteria: patients with ME, those with Gulf War Syndrome and patients with a definite history of exposure to organophosphate pesticides. We showed clear differences between the groups in terms of measured parameters, including muscle pain, and physical and mental status (Kennedy et al., 2004). Importantly, a high proportion of people in each group had measurable signs of muscle weakness in arms or legs, indicating that clinical signs can, in fact, be found in these patients if physicians take care to do a full physical examination. Future work will explore such important findings.

There have been other definitions apart from the CDC-1994 Fukuda one (see Figure 1). The most recent attempt to revise the definition (Carruthers et al., 2003) is based

on clinical experiences with very large numbers of patients. It will, however, be some time before this new "Canadian" description of ME/CFS replaces the CDC-1994 definition in clinical and research practice.

When comparing scientific studies, it is important to bear in mind that different definitions of ME/CFS may have been used, and this complicates interpretation and comparison of data. It can also be seen from the Figure below that there have been several attempts in the past decade to define diagnostic criteria for the illness. Each definition has been problematic, reflecting in part the special interest of the author, and taking little account of the extensive literature prior to 1988 (see Figure) that made the case for myalgic encephalomyelitis as a distinct clinical entity based on reports of epidemic and endemic cases.

What was this condition "Myalgic Encephalomyelitis" that existed before 1988, when it was subsumed within the "CFS" construct, and which is still referred to by patients in the lay literature as "ME"? Myalgic encephalomyelitis was first defined by Acheson (1959). It had been found to occur in epidemic and sporadic forms, and was believed to result from a continuing or persisting viral infection. It has been defined as a systemic illness, characterised by marked muscle fatigability (not just weakness); muscle

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Figure 2

Physiological and biochemical abnormalities found in "CFS" cohorts

Biochemical

Oxidative stress (*e.g.*, Richards et al., 2000; Manuel et al., 2001; Pall & Scatterle, 2001; Kennedy et al., 2003; Vecchiet et al., 2003)

Anti-viral dysregulation (*Suhadolnik et al.*, 1994; *De Meirleir et al.*, 2000; *Shetzline SE et al.*, 2002; *Tiev et al.*, 2003)

Vascular

Endothelial dysregulation (*Spence et al.*, 2000; *Khan et al.*, 2003; *Khan et al.*, 2004)

Brain perfusion (*Schwartz et al.*, 1994; *Costa et al.*, 1995)

Orthostatic Hypotension (*Streeten et al.*, 2000; *Stewart*, 2003)

Brain

Metabolic abnormalities (*Tomoda et al.*, 2000; *Puri et al.*, 2002; *Chaudhuri et al.*, 2003)

Muscle

Metabolism (*e.g.*, *Fulle et al.*, 2000; *Vecchiet et al.*, 2003)

Abnormal recovery after exercise (*e.g.*, *Paul et al.*, 1999; *McCully & Natelson*, 1999)

Enteroviral sequences in muscle (*Lane et al.*, 2003)

ME/CFS: a research and clinical conundrum

(continued)

pain, tenderness and swelling; variable involvement of the central nervous system (ataxia and cranial nerve involvement); muscle weakness and/or sensory changes due to neuronal damage; impairment of memory; sleep disorders, etc.; vascular involvement (orthostatic tachycardia, pallor); reticulo-endothelial dysfunction; and recurrences of flu-like symptoms with myalgia.

From 1934–90 there were at least sixtythree outbreaks of epidemic proportions, all well-documented, distributed geographically in North America (29 outbreaks), the UK (16), the rest of Europe (11), Australasia (4), Africa (2) and Asia (1). One of the most studied, and possibly the most controversial, of these outbreaks occurred at the Royal Free Hospital, London, in 1955, during which 292 people were affected. Indeed, outbreaks may still be occurring, and some of the patients who currently come under the CDC-1994 CFS definition have clinical features similar to the classical description of post-infectious ME patients defined above.

The fact that we are still aware of these details is in no small measure due to Dr J. Gordon Parish who is attending this workshop today. Dr Parish has over many years collected reports of these outbreaks of ME (Parish, 1978; Shelokov & Parish, 1989), and has a complete archive of the relevant literature.

A complete listing of these references can be found on the MERGE web site (www.mererearch.org.uk).

Given the heterogeneous nature of the term CFS, and the different ways of defining it, it is probably no surprise that many of the biomedical studies conducted into the illness — a relatively small number given the scale of the problem — have had inconclusive results. Despite this, however, a range of abnormalities have been found by a number of different research groups, and these are summarised in the Figure 2 (previous page).

Today's workshop will concentrate on the vascular and biochemical aspects of ME/CFS, but MERUK intends to facilitate further workshops concentrating on other aspects of ME/CFS pathophysiology, such as muscle metabolism and function, and neuro-imaging and brain function.

References

A full list of the references mentioned can be obtained from Dr Neil Abbot, ME Research UK (Charity Number SC036942), The Gateway, North Methven St, Perth PH1 5PP; e-mail meruk@pkavs.org.uk; website www.mererearch.org.uk

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*Based on a
presentation given at
the Royal Society of
Edinburgh Research
Workshop on ME/CFS*



Dr Vance Spence and Kathleen McCall and Sue Waddle from Invest in ME – at a presentation for Invest in ME entitled **Making the Breakthrough**

[<http://tinyurl.com/yreh7a>]

ME Story

*At work I have been
asked to go to see the
company doctor as no-
one believes I'm unwell
yet they see me
struggling to walk on
occasions! - Clare*

Facts About ME

*ME is estimated to cost
the UK economy over
£6 BILLION per year*

Biomedical Research into ME/CFS

Dr Vance A. Spence and Dr Neil C. Abbot

*Chairman of ME Research UK (charity number SC036942),
and Hon Senior Research Fellow, Institute of
Cardiovascular Research, University of Dundee, UK*



Specific research findings from the University of Dundee

As a supplement to the talks you are to hear during the IiME Conference 2007, this hand-out presents a brief overview of the recent research findings from the Vascular Diseases Unit in the University of Dundee,. One of the cardinal facts about research work generally is that breakthroughs follow funding (since without it there is no possibility of starting the exploration!). This group, with funding from ME Research UK, has uncovered several interesting findings in people with ME/CFS. These findings have been reported in a series of scientific papers published from 2003–2006.

a) Increased oxidative stress

In our experiments, we have found a pattern of significantly increased oxidative stress – increased oxLDL and isoprostanes with decreased HDL and GSH – in ME/CFS patients (Kennedy et al, 2004). As isoprostanes also act as vasoconstrictors, for ME/CFS patients their presence, accompanied by additional free radicals during exercise may be responsible for some of the symptoms – such as pain - seen after exercise. These findings have now been confirmed by at least four other research groups worldwide who have also shown excessive free radicals in blood, urine and muscle tissues of ME/CFS patients. *Isn't it important to discover the source(s) of these molecules, whether from excessive immune activity, chronic infections or abnormalities within muscle tissue?*

b) Abnormal acetylcholine metabolism

Acetylcholine is a substance produced by the layer of endothelial cells lining all blood vessels, causing them to open. Our group has found that vascular responses to acetylcholine are increased compared with matched control subjects (Spence et al 2000; Khan et al, 2004, a and b). This finding is in contrast with research into a wide variety of cardiovascular diseases – such as diabetes, stroke and high cholesterol – where blood flow responses to acetylcholine are normally blunted. *Why should 'CFS' patients have this seemingly unique thumbprint of increased*

blood vessel sensitivity to acetylcholine?

c) Increased neutrophil apoptosis

Also, we also have new data indicating that ME/CFS patients have detectable abnormalities in a type of white blood cell (called neutrophil) – specifically a larger proportion of dying (apoptotic) cells than in healthy subjects – consistent with an activated inflammatory process which is possibly the consequence of a past or present infection (Kennedy et al 2003, 2004a). Accompanying these markers of neutrophil apoptosis, we found that high-sensitivity C-reactive protein levels, recognised as a marker of the inflammatory process, were also significantly increased. *Might some people with 'CFS' have a chronic inflammatory disorder, albeit an unusual one?*

d) Presence of "signs" of physical illness

Importantly, a high proportion of the patients investigated in this unit have had measurable signs of muscle weakness in the arms and/or legs, indicating that clinical signs (rather than self-reported symptoms) can, in fact, be detected in these patients if physicians take care to do a full physical examination (Kennedy et al 2004b). Intriguingly, reports in the older literature (1950s and 1960s) on epidemics of 'classical' ME included the presence of clinical signs (e.g., muscle weakness/swelling; sensory nerve changes; observable recurrences of flu-like illness, etc). *Will the presence of clinical signs - believed by many healthcare professionals today to be non-existent in ME patients - come to be recognised as important markers of physical illness?*

Our purpose here is not to *answer* these questions, but to show that biomedical investigation can uncover, within a proportion of ME/CFS patients, biological anomalies that might well help to explain many of the clinical features associated with the illness, and might also indicate areas for therapeutic treatment.

(continued on page 20)

Biomedical Research into ME/CFS (*continued*)

General research findings from groups worldwide

For the first time in many years, there is optimism about the potential for biomedical advances in ME research. A range of groups are beginning to report physiological abnormalities in many patients with ME/CFS, showing what can be achieved if **scientific effort** and **funding** are targeted towards **biomedical** research, leading to therapeutic intervention and treatment. The Table below (from ME Research UK's report of the Royal Society of Edinburgh/Wellcome Trust workshop on ME - available on our website) lists some recent areas of progress that may prove to be important.

The Future?

All these results are very exciting, and they may well help us to explain some of the unusual symptoms that these ME/CFS patients experience. It is also important to recognize, however, that these tests are not diagnostic markers. We are currently formulating new hypotheses and designing new

experiments in order to unravel the significance of acetylcholine sensitivity, increased oxidative stress, increased early death of neutrophils etc, in the ME/CFS patients. Experience has convinced us, however, that funding will be difficult to maintain, and that the funding strategy for ME must mirror that of cancer research which obtains 85-90% of its revenue from private sources and ground-level fundraising. It is a huge task, but much can be achieved by a **determined and collaborative** ME community.

References

A full list of the references mentioned can be obtained from Dr Neil Abbot, ME Research UK (Charity Number SC036942), The Gateway, North Methven St, Perth PH1 5PP; e-mail meruk@pkavs.org.uk;

website www.mereseearch.org.uk

Table: Physiological and biochemical abnormalities found in groups of ME/CFS patients.

BIOCHEMICAL	Oxidative stress (Richards 2000 et al. ; Manuel 2001 et al.; review by Pall 2001; Kennedy et al. 2003; Vecchiet et al. 2003)
	Dysregulation of anti-viral pathways - i.e. abnormal activity of the anti-viral immune responses (Suhadolnik RJ et al. 1994; De Meirleir et al. 2000; Tiev et al 2003)
VASCULAR –	Endothelial dysregulation - i.e. abnormal responses of small blood vessels selectively to acetylcholine (Spence et al. 2000; Khan et al. 2003 and 2004)
	Altered brain perfusion i.e. areas of reduced blood flow in the brain (Ichise et al 1992; Costa et al. 1995; Tirelli et al. 1998)
	Orthostatic hypotension i.e. physiological changes to blood pressure/cardiovascular mechanisms on standing (Streeten et al. 2001; Naschitz et al. 2002; Stewart et al. 2003)
BRAIN	Metabolic abnormalities e.g. alterations of brain choline (important in brain function). (Tomoda et al. 2000; Puri et al. 2002; Chaudhuri et al. 2003)
MUSCLE	Altered metabolism - e.g. changes in muscle composition or use of fuel. (Fulle et al. 2000, Vecchiet et al. 2003, Fulle et al. 2003)
	Abnormal response to exercise (Lane et al. 1998; Paul et al. 1999; McCully et al. 2004).
	Enteroviral sequences in muscle - i.e. evidence of a persisting virus in some CFS patients (Lane et al. 2003; Douche-Aourik F et al. 2003)

The Strategy of the Medical Research Council for Research on CFS/ME

By Professor Colin Blakemore
Chief Executive, Medical research Council

The development of MRC's CFS/ME Strategy

Following the publication of the Report of the Chief Medical Officer's Independent Working Group in 2002, the MRC convened a CFS/ME Research Advisory Group (the Membership and Terms of Reference of which appear in [Annex 1](#) below). This Group was asked to advise the MRC on a broad strategy for advancing biomedical and health services research on CFS/ME.

The Advisory Group met three times between September 2002 and March 2003, and also undertook a consultation exercise, in July and August 2002, using a set of structured questions. The results were independently analysed by the NHS Public Health Resource Unit, Oxford. The lay members of the MRC CFS/ME Research Advisory Group met with ME charities, CFS/ME patients and their carers, in order to improve understanding of their perspectives. A preliminary draft research strategy was made available to key stakeholders, as well as national and international researchers, for external, open consultation. It was also considered by the MRC Research Boards between December 2002 and February 2003. The preliminary draft research strategy was revised by the MRC CFS/ME Research Advisory Group in the light of the results of this consultation, and the final version was presented to the governing body of the MRC, its Council, in March 2003.

In May 2003 the MRC published the report of the independent Research Advisory Group. The report can be viewed or downloaded from the MRC website:

(<http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC003412>).

The Research Advisory Group agreed that the research community should be encouraged to develop high-quality research proposals addressing key issues for CFS/ME research in areas that were considered amenable for study at the present time. In particular, the Group drew attention to the potential for progress in certain areas, for instance in research that addresses:

- the understanding of symptomatology
- improved case-definition
- new approaches to management.



Invest in ME had invited Professor Blakemore to speak at the IiME International ME/CFS conference but unfortunately he was not able to make it. The MRC were invited to send another speaker, and were offered the chance to send representatives to attend as delegates, but these offers were also declined.

The MRC CFS/ME Research Advisory Group concluded that there is probably a multiplicity of potential causal factors for CFS/ME and they reviewed the widely disparate results of research so far reported in the scientific literature concerning the biological basis of the condition. They concluded that, as in many other areas of medical progress, valuable treatments might be developed and tested, even if there is not a full understanding of the triggers and causal pathways that lead to CFS/ME. Therefore, the Advisory Group recommended to the MRC that the most likely route to rapid help for patients was through support for research on interventions for CFS/ME, even while there remains incomplete knowledge of its causes and underlying pathogenesis. This recommendation does not debar the consideration of applications exploring the mechanism and aetiology of the condition, if high-quality proposals can be developed.

The MRC does not normally set aside specific amounts of money for particular illnesses, not

(continued on page 22)

MRC Strategy for Research on CFS/ME (*continued*)

even for the most common conditions, although in areas of serious unmet clinical need, we do sometimes issue highlight notices, to alert the research community to our strong interest in funding good research. The MRC issued such a highlight notice for CFS/ME and that highlight notice is still in effect. Thus, the MRC continues to encourage research applications in CFS/ME, and our Research Boards have agreed to prioritise this area. However, applications must not fall below the scientific standards set by our rigorous peer review process, through which applications are judged in open competition with other demands on funding. The main factors in our Research Boards' funding decisions are:

- research excellence;
- the likelihood of major advances in knowledge; and
- the clinical importance of the topic.

This is to ensure that the research supported by the MRC will have the best chance of delivering knowledge that will be useful in tackling medical conditions, and that we therefore use taxpayers' money to good effect. Needless to say, the MRC has a responsibility to encourage the strong UK research community to contribute as widely and effectively as possible to improving the health of the nation. So, the MRC is very keen to support high-quality studies on CFS/ME that stand a good chance of delivering their stated aims. It would obviously not be acceptable to the public as a whole for the MRC to support research applications that are judged, in open competition, to be of lower quality than other proposals that are more likely to yield results of real value to the sufferers of other conditions.

Challenges to understanding the causes and biological bases of CFS/ME

There are a number of challenges to advancing the understanding of CFS/ME arising from individual variation in the spectrum of signs and symptoms associated with fatigue conditions, and hence uncertainty about the cardinal signs of CFS/ME. A related problem in the design of research is the variability of response of sufferers to potential interventions, possibly because of differences in underlying aetiology and pathology.

The intensity as well as the nature of the symptoms vary considerable, not only between patients but also over time for individual patients, and at different stages in the progress of the condition. The lack of consistency of data from experiments on people with CFS/ME presents a huge challenge to the interpretation of the results of research. The fact that some, perhaps many patients have one or more other comorbid conditions, particularly mood and anxiety disorders, makes research even more difficult. The complexity of this condition led the Advisory Group to recommend that researchers should develop high-quality research proposals addressing key issues for CFS/ME research that are amenable for study at the present time.

It is hoped that improved definition of the phenotypes of potential subgroups that may come under the CFS/ME spectrum, will help to underpin future research on causes and mechanisms. However, the MRC remains committed to funding scientific research into all aspects of CFS/ME at any time and will consider funding research into the biological basis of the condition, provided it meets the quality thresholds set out above.

Another challenge for CFS/ME is the lack of researchers with an adequate understanding of the condition and training in the multidisciplinary approaches that might facilitate ground-breaking discoveries.

Unfortunately, the openly expressed frustration of many CFS/ME sufferers has led many researchers to feel under attack from the very community that they are trying to help. The frustration, even hostility, expressed against researchers can only discourage the necessary influx of new researchers to take the field forward.

Current MRC funding for CFS/ME

The MRC is currently funding six research projects on CFS/ME (see Annex 2) – a total investment of more than £3m. For comparison, this is similar to the level of MRC support for research on autism and on skin cancer. The MRC's portfolio includes two large clinical trials of new approaches to treating CFS/ME – the PACE trial (£2,076,363) and the FINE trial (£824,129). The PACE trial will be comparing three treatments given to patients in a clinical setting, one of which is Adaptive Pacing Therapy (APT). This

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MRC Strategy for Research on CFS/ME (*continued*)

treatment is popular with many patients but has not been scientifically evaluated before. With the help of Action for ME, APT has been adapted to enable the researchers to test it rigorously within the trial. The FINE trial will also test three different treatments. They are delivered to patients at home by specially trained nurses, so are particularly suitable for patients who are too ill to attend a specialist clinic.

Conclusions

The MRC recognises the scale of suffering caused by the spectrum of disorders characterised by fatigue and wants to use public funds sensibly and productively to help CFS/ME patients. We maintain our highlight notice as an indication of the priority that we attach to this area, and we shall support research on any aspect of CFS/ME that is of high quality and is likely to lead to real advancement of knowledge.

Colin Blakemore

Chief Executive, Medical Research Council

April 2007

Annex 1

MRC CFS/ME Research Advisory Group & Terms of Reference

Chair :

- Nancy Rothwell, University of Manchester
- Jacqueline Apperley, MRC Consumer Liaison Group
- Philip Cowen, University of Oxford
- Janet Darbyshire, MRC Clinical Trials Unit
- Diana Elbourne, London School of Hygiene and Tropical Medicine / Institute of Education
- Sue Haslehurst, MRC Consumer Liaison Group
- Alan McGregor, Guy's, King's and St Thomas's
- Jon Nicholl, University of Sheffield
- Jackie Oldham, University of Manchester
- Chris Verity, Addenbrooke's Hospital
- Jonathan Weber, Imperial College School of Medicine
- Til Wykes, Institute of Psychiatry

Note: All members of the MRC CFS/ME Research Advisory Group acknowledge that inevitably in their professional or personal life they may have indirect connections with individuals who may have undertaken research in this area, or who either themselves or a family member may have or have had CFS/ME. The Group agreed there to be no conflict of interest in such cases.

Observers / Secretariat

- Susan Lonsdale, Department of Health
- Chris Watkins, Medical Research Council
- Elizabeth Mitchell, Medical Research Council

The Terms of Reference for the MRC CFS/ME Research Advisory Group

- To consider the Report of the CMO's Independent Working Group on CFS/ME, including its recommendations for research,
- To consider other recent reviews of current knowledge and understanding of CFS/ME,
- To take account of patient and lay perspectives,
- To recommend to MRC a research strategy to advance understanding of the aetiology, epidemiology and biology of CFS/ME and,
- In the light of current knowledge suggest what areas of further research are needed with regard to possible prevention, management (including diagnosis) and treatment.

The MRC CFS/ME Research Advisory Group agreed not to revisit the areas considered by the CMO's Independent Working Group, but to recommend how research might be undertaken that would improve understanding and treatment of CFS/ME. It was agreed that it was beyond the remit of the Research Advisory Group to decide how the recommendations for a research strategy should be implemented, since this would be the responsibility of funders and sponsors.

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MRC Strategy for Research on CFS/ME (*continued*)

Annex 2 - Current MRC support for CFS/ME research

		04/05 Expenditure	05/06 Expenditure
Peter Denton White, G0200434 The PACE trial; A RCT of Cognitive Behavioural Therapy, graded exercise, adaptive pacing and usual medical care for chronic fatigue syndrome, Queen Mary and Westfield College, St Barts Hospital (Trials Grant)	Intervention study	£244,791	£459,208
Alison Joan Wearden, G0200212 Randomised controlled trial of nurse led self-help treatment for primary care patients with chronic fatigue syndrome, University of Manchester, (Trials Grant)	Intervention study	£159,809	£187,488
Richard K Morriss, G0100809 Exploratory RCT of training General Practitioners to manage patients with persistent Medically Unexplained Symptoms (MUS), University of Liverpool, (Trials Grant)	Intervention study	£154,777	£83,925
Kamaldeep Bhui, G0500978 Chronic Fatigue & Ethnicity, Queen Mary and Westfield College, St Barts, London (Research Grant, New Application)	Epidemiology	-	-
Francis Creed, G0500272 The feasibility of a population based study of CFS, IBS and CWP, University of Manchester (Research Grant, New Application)	Epidemiology	-	£21,302
Total expenditure figures		£559,377	£751,923
Related grant			
Michael Sharpe, G0300876 A complex intervention for patients with medically unexplained symptoms in neurology clinics: Trial platform		£57,977	£118,756
Total, including Sharpe		£617,354	£870,679

ME Story

The psychiatrist visited Sophia for 20 minutes one morning.

The psychiatrist gave her no physical examination, which I found strange, given that her blood pressure was 80/60 and was unable to understand that Sophia's "clock" was constantly on the move and that mostly her day-time was in our night-time.

The psychiatrist did not seem to understand any of her myriad symptoms and the following day gave a lecture on M.E. to a large number of doctors; never having asked Sophia for her consent.

The psychiatrist wanted me to be present, though I had reservations, and gave everyone there a handout about Sophia and our family, (which I only received later as part of the pack of Sophia's notes). It read like a novel with some horrendous so called "facts" that I did not recognise as a true representation. I was also shocked at the misrepresentation of Sophia's symptoms to the doctors and started to object, at which point I was ushered out of the room.

(from **The Story of Sophia and M.E.** –

<http://www.investinme.org/Article-050%20Sophia%20Mirza%2001.htm>)

The UK FINE Trials – A view from a Participant

FINE Trials - Set Up & Objectives

These trials are funded by the Medical Research Council (MRC) alongside another set of trials called PACE trials. Both are described by the MRC^[1] as

'..complementary trials into various treatments options for CFS/ME which aim to improve quality of life for those who are ill.'

'FINE (Fatigue Intervention by Nurses Evaluation) will test two different treatments that are particularly suited to those who are too ill to attend a specialist clinic.'

'The FINE trial will involve patients in the North West of England and North Wales.'

The recruitment of patients for both trials was started in 2004 and, according to the MRC, were expected to take up to five years to complete.

The FINE trials are headed by Dr. A. Wearden from Manchester University whose background is rehabilitative therapy.

FINE treatments would be delivered in patients' own homes (*'so the trial is particularly suited to those who are too ill to attend specialist clinics.'* – according to the MRC)

Inclusion Criteria

The MRC claims that the trials will use the most inclusive criteria for CFS/ME to determine eligibility to take part (the Oxford criteria) in order for the results to be generalised to the largest number of people possible.

FINE TRIAL COSTS

The FINE trials cost £1,147,000.

FINE Trials - EXPERIENCE

by Alice

I have been phoning the trial office but no answer yet!

I want to withdraw (from the FINE trials) for a whole load of reasons. I will try to explain some of them here but may not make much sense due to brain-fogginess so please excuse that.

Reasons:

- 1 Data they collected about me was misleading. Only questionnaires were used in the 2 sessions I had with the researchers and the questions were leading and did not reflect my true feelings. Also the researchers spent 2-3 hours with me each time which was so exhausting that I think I didn't really know what my replies were.
- 2 The trial totally disregards ME/CFS as an illness. It is based on a theory that our symptoms are due to deconditioning and maladapted beliefs about exercise. I was initially suspicious of this but agreed to it because it provided me with a lifeline (was great for me to believe I could get better through exercise) and also because in the initial session the nurse gave me a presentation which lasted over three hours. I was so exhausted. The disregard of the illness was reflected on a practical level. For example, they said that if I recover from exercise in ten minutes then I am working at the right level. I abided by this rule and later crashed due to delayed and accumulated effects (which are widely accepted features of this illness). How this is ethical I do not know!
- 3 **The program was hypocritical.** They had strict rules for me to live by regarding pacing (yet gave me very little practical advice on this). Yet they felt it was okay to do 3 hour long sessions with me! It felt unworkable.
- 4 **I crashed after the last session with them,** so although my report was not glowing, it is highly misrepresentative of the actual outcome (probably my most important point)!! I am now worse than I have been in the duration of this condition.
- 5 **The therapist who provided the intervention had very selective hearing** and she would adapt whatever I said to fit into what she wanted to hear (I have examples of these but won't bore you).
- 6 **The therapist was critical of me and unsupportive.** She was defensive when I questioned things.

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7. **I believe the consent process was unethical.** I was not aware what I was letting myself in for. (they did not explain the details of the intervention until after I had consented). In addition, the deconditioning theory was presented as fact and there was no mention of a balanced viewpoint (I have since read research that goes against this deconditioning theory).
8. **Another example of my data not being represented properly:** I suspended from University a couple of weeks before the start of the program and had started to improve from the rest. I continued to improve for a little while into the program. I made sure I highlighted that the cause of this improvement could be the effects of the program, or the rest I was getting. They were not interested in this - the fact that there was basically another aspect of my life that could be causing changes in my condition.

I was unhappy during the study but wanted to continue because I thought (stupidly) that in some small way I was helping the fight against ME. It is in realising that my data will probably be used in some way to support this program - that I feel made me so much worse - that makes me want to withdraw.

Blimey, I have written all this and still don't feel like I've painted the picture.

The doctor put me forward for this trial because this was all he knew of to do. I so wish I had done my research first. I will be so much more cautious in the future.

It frightens me to think that this research will be used to support clinics offering this in the future.

Anyway, I hope that is of help to someone. I can provide more information if anyone is interested.

Thanks for your replies and I hope this is a good day for you.

Alice x

ME Story

Even if it had been the right treatment, by that time it was too late: so many years of neglect, disbelief, wrong medication, wrong diagnoses; so many times referred to psychiatrists, who to a man sent her away because they couldn't find anything wrong - with a prescription for an anti-depressant just in case.....

- Richard

ME Story

*How do I deal with family that say things like "stop researching that...don't you think your just wallowing in it just the more?"
How do you stop looking for answers? When is it time to give up? Why don't people that have known you all their lives...know you and what your suffering is REAL?? Why do doctors still say this doesn't exist and yet look at many of us ...completely destroyed by this disease.....*

- Cynthia

ME Story

When I try to get medical care, the strain of trying to convince someone I am ill and the hurtful things they say to me practically make me crack up. Just the physical demands of leaving the house, even in the wheelchair, are enough to make me sicker for weeks. I can't describe how ill it makes me feel - Shannon

ME Story

Despite strenuous efforts on my part to keep well and fulfil my duties to the best of my capabilities, I suffered a complete collapse in September, 2003 and was almost bed-bound for many months.

I have been unable to work full-time since then and even very small, part-time jobs cause the flu-symptoms, severe headaches, blackouts, loss of balance, nausea, weak limbs, IBS, brain-fog and exhaustion to start up again. I'm one of the lucky ones.... -

Daphne

Jane Colby

Invest in ME are happy to work with other groups and charities for the benefit of people with ME and to make progress regarding the urgent issues which need to be tackled. Our recent campaign to have ME recognised as a notifiable illness in schools was initiated from the work performed by Jane Colby. Jane is a former head teacher who has ME and who formed Tymes Trust. It is now ten years since Jane and Betty Dowsett published their work. Here Jane recalls a historic day for children with ME and describes the day that the term ME Plague was coined.



Invest in ME book 2007 - "Schools swept by ME Plague"

On 12th May, ME Awareness Day 2006, I was honoured to speak on 'Children with ME' at the Invest in ME Conference. I called for ME to be made notifiable due to its encephalitic symptoms and I am delighted that Invest in ME have since been campaigning for this. I was then invited to write a Review for the *Journal of Clinical Pathology*, called *Special Problems of children with ME/CFS and the enteroviral link*, it can be read online at www.cfids-cab.org/rc/Colby.pdf and in the printed Journal. On ME Awareness Day 2007 I am in a very different venue - Brentwood Cathedral - for our *Remember the Children* concert.

But 10 years ago it was the 22nd May that caused a storm, when the headline above was splashed across *The Guardian* front page. I had no idea how big my joint research with Dr Betty Dowsett, a legend in her own lifetime, would become. I'd pre-recorded interviews for the morning television news and was booked for radio news shows, but as the phone rang constantly while I tried to get ready, and I had to use my fax to make outgoing calls, I began to get the message. Dr Dowsett went to ground like Badger in *Wind in the Willows!*

Arriving at the studios at 7.45am I was asked: "Have you seen *The Guardian*?" I hadn't. Then I was asked to fit *The Today Programme* in between the others. Guest Simon Wessely was saying: "I'm sure Jane would agree..." I didn't, and I'm afraid I ignored his question. There was too much else to discuss. Mainly the fact that ME had just been revealed as the key reason for children and young people missing school long-term due to illness. ME was causing over half of all long-term sickness absence, almost twice that of cancer and leukaemia combined (51% against 23%). Getting the figures had taken five years. We studied a school roll of a third of a million children and over 27,000 staff. Not easy to ignore, although the *British Medical Journal* discouraged the profession from giving it credence. Six months later, however, it published a 450 word letter from Dr Dowsett and myself, choosing the headline: 'Journal was wrong to criticise study in schoolchildren'.

At this distance in time it is easy to forget that it was a school epidemic that sparked off our study. What was the pattern in other schools, we wondered? Almost 40% of cases we uncovered were in clusters of 3-9 and 21% were in pairs. The clusters involved staff and pupils. We found a prevalence of 70:100,000 in pupils and 500:100,000 in staff. Associated with the clusters were other long term absences caused by viral illness, not yet diagnosed but often described as gastro-intestinal or flu-like. (Enteroviruses, the suspected culprits in many cases of ME, produce both these symptom profiles.) We concluded that the early investigation of infective agents associated with such a serious illness in schools should be instigated, and we recommended this. To our knowledge, nothing has been done.

I feel another campaign coming on... You can read all the results of the survey as described by Dr Dowsett at www.tymestrust.org/pdfs/dowsettcoby.pdf

PROFILES of PRESENTERS at the IiME INTERNATIONAL ME/CFS CONFERENCE

Norman Lamb MP Member of Parliament for North Norfolk, Liberal Democrat Shadow Health Secretary



Norman Lamb entered Parliament at his second attempt in 2001, gaining this seat from the Conservatives.

Norman Lamb read law at the University of Leicester. He worked for Norwich City Council as a senior assistant solicitor before joining Norfolk solicitors Steele and Co., where he became a partner and head of the firm's specialist Employment Unit.

He worked for a year as a Parliamentary Assistant for Greville Janner, QC, MP. He was a member of Norwich City Council 1987-91, leading the Liberal Democrats for the last two years of his term. He has built a strong reputation in Norfolk as a campaigner for improved health services. He has been a critic of cuts in bed numbers and has highlighted the resulting unacceptable level of cancelled operations.

As an MP his work on local issues includes adjournment debates on: orthopaedic waiting times in Norfolk; the lack of school transport services in North Norfolk; police funding in Norfolk; funding for Further Education Colleges; the provision of care for people with dementia; and coastal erosion.

Norman has been Lib Dem Deputy Spokesperson for International Development (2001-02), a Treasury spokesman (2002-03), PPS (Parliamentary Private Secretary) to Charles Kennedy (2003-05) and Shadow Trade and Industry Secretary (2005-06). He was a principal author of the party's policy on Royal Mail.

From March to December 2006, Norman was Chief of Staff for party leader Sir Menzies Campbell. In December 2006 he was appointed Liberal Democrat Shadow Health Secretary.

He has a particular interest in Africa: he has led Adjournment Debates on the HIV/AIDS crisis facing Africa and Asia, the controversial sale of military air traffic control system in Tanzania and the situation in the Great Lakes region of Africa.

Dr. Derek Pheby - Project Coordinator, National ME Observatory, and Senior Fellow, University of Hull

Dr Derek Pheby is an epidemiologist, and was Director of the Unit of Applied Epidemiology at the University of the West of England, Bristol. He has a long-term interest in ME, and was a member both of the National Task Force on ME and of the Key Group of the Chief Medical Officer's Working Group on CFS/ME. His unit had an active programme of research into chronic fatigue syndrome and ME. Dr Pheby is a member of the Editorial Board of the International Journal of Chronic Fatigue Syndrome.

Dr. Jonathan Kerr

Jonathan Kerr was born in Belfast in 1963, qualified in medicine from Queen's University of Belfast (1987), and completed training as a medical microbiologist (1995).

He has worked as a microbiologist in Belfast, Manchester and London, taking up post as a Consultant Senior Lecturer in Microbiology at Royal Brompton Hospital / Imperial College in June 2001, and then Sir Joseph Hotung Clinical Senior Lecturer in Inflammation at St George's University of London in 2005.

His interest in Chronic Fatigue Syndrome (CFS) began during a study of the consequences of parvovirus B19 infection, when he showed that a percentage of infected cases developed CFS which persisted for several years.

He is now the principal investigator in a programme of research in CFS. This involves development of a diagnostic test using mass spectrometry, analysis of human and viral gene expression in the white blood cells, and clinical trials of immunomodulatory drugs.

Dr. Jonathan Kerr and colleagues at St. George's University of London reported in the July 27, 2005 issue of the Journal of Clinical Pathology that a preliminary study of 25 CFS patients and 25 matched healthy controls revealed abnormalities in 35 of 9,522 genes analyzed using microarray technology. Polymerase chain reaction studies showed the same results for 16 of these genes.

The study, and its results, raises some important questions. The first of which pertains to the need for funding of microbiological CFS research. He is funded (>£1million) by the CFS Research Foundation (www.cfsrf.com), a charitable organization based in the U.K., and leads a group of 5 scientists at St George's.

The Foundation needs private support to continue their research efforts. They also openly post the results of their efforts on their website <http://www.cfsrf.com>.

**Dr. Ian Gibson
MP for Norwich North**

Dr. Ian Gibson has been the MP for Norwich North since his election in 1997.

He is originally from Scotland and was born in Dumfries on the 26th September 1938.

He went to school at Dumfries Academy and acquired a passion for all things scientific- especially biology.

He pursued his passion for science by going on to study at Edinburgh University where he gained a BSC and later on a PhD in genetics.

He served as the Dean of the School of Biological Sciences at UEA from 1991 to 1997 and headed a research team investigating various forms of cancer, including leukaemia, breast and prostate cancer. In 2003, the university made Fr. Gibson an Honorary Professor.

Dr. Gibson first stood for Parliament in 1992. Although losing that election by just 266 votes he tried again in 1997 and won the Norwich North seat by 9470 votes. He has been re-elected twice since 1997- in 2001 and most recently in May 2005.

His work in Parliament and in Norwich has primarily consisted of advocacy work and pushing the government to take more notice of the role that science plays (and can play) in the UK. His scientific background has meant that he has been involved in numbers of groups and charities in Parliament.



Professor Hooper

Professor Hooper graduated from University of London and had held appointments at Sunderland Technical College, Sunderland Polytechnic and the University of Sunderland, where he was made Emeritus Professor of Medicinal Chemistry in 1993.

He has served at many UK universities as well as in India and Tanzania. He has inaugurated links with Indian research institutions and universities and celebrated

25 years of productive and on-going links which have, particularly, involved the design and development of new drugs for tropical diseases and an exploration of natural products associated with Ayurvedic medicine. He has published some 50 papers in peer-reviewed journals in the field of medicinal chemistry together with major reviews on the Chemotherapy of Leprosy, the Chemistry of Isatogens. Edited one book on the Chemotherapy of Tropical Diseases.

He acted as a referee for a number of important journals and served on one editorial board. He has served on committees of the Council for National Academic Awards (CNAA), the World Health Organisation (WHO) and the Science and Engineering Research Council (SERC).

Professor Hooper is a member of a number of learned bodies, including the Royal Chemical Society, the British Pharmacological Society and the Society for Drug Research (SDR), now renamed the Society for Medicines Research, where he has served on the committee for 12 years and served as Chairman for 2 years. This involved the planning and organising of major national and international conferences. He was appointed Chief Scientific Advisor to the Gulf Veterans Association (GVA) and accepted by the Ministry of Defence (MoD) as their nominee on the Independent Panel established to consider the possible interactions between Vaccines and NAPS tablets.

He has also served on the Gulf Support Group convened at the Royal British Legion. His involvement with the GVA brought contact with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/M.E.) and related disorders. Gulf War Illness/Syndrome (GWI/S) has much in common with M.E./CFS.

He is Patron of the Sunderland and South Shields M.E. Association and a member of the Newcastle Research Group, which includes eminent physicians and scientists performing research in to CFS/M.E., where one recent aspect has been the identification of organochlorine pesticide poisoning being misdiagnosed as M.E./CFS.

He has addressed meetings of the Pesticide Exchange Network and consulted to the Organo-Phosphate Information Network (OPIN).

He worked with the Autism Research Unit (ARU) at the University of Sunderland for over 20 years, leading to involvement in biochemical studies to offer help, support and treatment for people with autism. This has also lead to research and urine-analysis of Indolyl-Acroyl-Glycine (IAG), which is an unusual metabolite found in excess of 90% of people examined in different groups of GWV,

M.E./CFS and Organo-Phosphate (OP) poisoning sufferers. He served on the General Synod of the Church of England from 1970 to 1980 and he is a Christian Lay Leader, Preacher and Teacher.

He is currently involved in three environmental campaigns:

- Toxic waste dumping, including campaign against sewage in the sea presenting to the Select Committee on Sewage Treatment and Disposal
- GWI/S, presenting to the Defence Select Committee
- M.E./CFS and OP/Pesticide poisoning



Dr. Abhijit Chaudhuri

Dr. Chaudhuri was appointed as a Senior Lecturer and Consultant Neurologist in July 2000. Research on fatigue in common neurological disorders is the main theme of Dr. Chaudhuri's work. He takes special interest in myalgic encephalomyelitis (ME).

His other areas of interest are multiple sclerosis, neuroimmunity, neurological infections and adult neurometabolic diseases.

Dr. Chaudhuri was responsible for examining spinal tissue from [Sophia Mirza](#) prior to the [inquest into Sophia's death](#).

Professor Kenny De Meirleir

Dr. De Meirleir is a world renowned researcher and is professor of Physiology and Internal Medicine at Free University of Brussels in Belgium. He is co-editor of Chronic Fatigue Syndrome: A Biological Approach, co-editor of the Journal of Chronic Fatigue Syndrome, and reviewer for more than 10 other medical journals. Dr. De Meirleir was one of four international experts on the panel that developed the Canadian Consensus Document for ME/CFS. He assesses/treats 3,000 to 4,000 ME/CFS patients annually.

Professor Kenny L. De Meirleir, MD received his medical degree at Vrije Universiteit Brussel, Magna cum laude. His research activities in Chronic Fatigue date back to 1990. His other research activities in exercise physiology, metabolism and endocrinology have led to the Solvay Prize and the NATO research award. He is director of the Human Performance Laboratory and Fatigue Clinic at the Vrije Universiteit Brussel, as well as consultant in the Division of Cardiology and director of the cardiac rehabilitation program at Vrije Universiteit Brussel. [4/10/01]

Dr. Daniel Peterson

Dr Peterson is an affiliate of the Sierra Internal Medicine Associates in Incline Village, Nevada; ME/CFS researcher and clinician; a board member of the American Association for Chronic Fatigue Syndrome; and member of the International Chronic Fatigue Syndrome Study Group.

Dr. Daniel Peterson was one of the two physicians who identified the original outbreak of CFS in Incline Village, Nevada, in 1984.

Dr. Vance Spence

Dr. Spence is a graduate of the Universities of London and Dundee. He was a Principal Clinical Scientist responsible for vascular services and research and, in 1997, he rejoined the University of Dundee Medical School as Honorary Senior Research Fellow in the Department of Medicine, with the objective of stimulating research into the causes of ME.

Dr. Spence was instrumental in the founding and launching of ME Research UK.



Mrs. Annette Whittemore

Reno resident Annette Whittemore is President and Co-founder of the foundation.

She became active in starting the foundation because she is the parent of a young adult who was severely affected by CFS and HHV-6 for the last 15 years.

She and her husband are business owners and philanthropists in Reno and Sparks.



She started the foundation with Kristin Loomis from California after a brief meeting in Incline, NV. with Dr. Daniel Peterson, a leading clinical researcher in CFS and HHV-6. "We wanted the ability to stimulate communication and research into the cause and effects of this illness. We've both felt the frustration of seeing too many doctors who could not help," she said. "Unfortunately for the sufferers of this disease, there have been very few doctors who have been able to understand the severe disability that HHV-6 and CFS can cause. By bringing world class researchers together we hope to unravel the path of this disease and develop new therapeutics while searching for a cure."

Annette's husband Harvey is a prominent attorney and developer who is currently developing Coyote Springs a 43,000-acre master planned golf community in southern Nevada. Harvey and Annette are both supporters of the University of Nevada's academics and athletics, with a particular interest in the future Knowledge Centre on the Reno campus. The couple is also actively involved philanthropically with several churches and community organizations.

Dr. Byron Hyde

Dr. Byron Hyde attended the Haileybury School of Mines and worked as a geophysicist. He then did premedicine in the Faculty of Medicine and University College, University of Toronto, obtaining a degree in chemistry and nutrition.



He graduated in medicine from the University of Ottawa where he was the Director and Chief of the International Exchange Program for the Canadian Association of Medical Students and Interns (CAMSI). Dr. Hyde founded the International Summer School in Tropical Medicine. He interned at Hotel Dieu in Montreal, was a resident at St. Justine Hospital in Montreal and at the Ottawa Civic Hospital. He also studied in Munich at the University Kinderklinik and in Paris at the Necker Hospital for Children. He was a research chemist at the Roscoe B. Jackson Laboratory at Bar Harbour, Maine, a leading world laboratory in immunological research. Following this, he was Chief Technician in charge of the Electron Microscope Laboratory in Toronto at the Hospital for Sick Children, followed by a similar post at the University of British Columbia.

Dr. Hyde has authored a book on Electron Microscopy and two non-medical books. Dr. Hyde has been a physician for 25 years and has performed charitable work as a physician in Laos and the Caribbean.

He held the position of Chairman of the Ottawa Community Health Services Association, and is presently Chairman of The Nightingale Research Foundation. In 1984, Dr. Hyde began the full-time study of the disease process then known as Myalgic Encephalomyelitis (renamed in 1986 by Dr. Gary Holmes in the USA to Chronic Fatigue Syndrome). He has worked exclusively with M.E./CFS patients since 1985.

In 1988, Dr. Hyde organized an association and founded The Nightingale Research Foundation, dedicated to the study of Myalgic Encephalomyelitis / Chronic Fatigue Syndrome. He has also acted as Chairman of the 1990 Cambridge Easter Symposium and of the Workshop on Canadian Research Directions for Myalgic Encephalomyelitis / Chronic fatigue Syndrome in May, 1991, at the University of British Columbia. (The above was extracted from the Nightingale Foundation website)

Dr. Sarah Myhill

Dr. Myhill is a general practitioner with a particular interest in chronic fatigue syndrome. She qualified from Middlesex Hospital Medical School with honours in 1981 and has worked in the NHS and in private practice.

Dr. Myhill is an active figure in the British Society of Allergy, Environmental and Nutritional Medicine, and its Secretary and has been medical advisor to Action for ME.

Dr Myhill is interested in diagnosis in the correct sense, finding the cause of illness, not simply in treating the symptoms.

She has a special interest in treating chronic fatigue syndrome (CFS) and have consulted over 100 farmers with CFS following organophosphate poisoning and 100 women with CFS following silicone poisoning either from breast implants or injection.

Over the past twenty years Dr. Myhill estimates to have seen over 1,500 cases of chronic fatigue syndrome largely caused by viral infection. During the early years she reported these cases individually to the Medical Devices Agency.

**Ellen Piro**

President Norwegian ME Association

Ellen Piro is the president of the Norwegian M.E. Association.

In 1995 she circulated a worldwide petition to get the CFS name changed and she personally brought it to the Dublin CFS conference to urge the scientists to make a change.

Recently Ellen has been involved in the investigation into the use of meningitis vaccines in Norway and New Zealand and which has ben connected with the cases of over 250 ME patients.

She has also contributed to the debate on the Norwegian equivalent of the NICE guidelines.

**Dr. Nigel Speight** Consultant Paediatrician at Durham University Hospital

Working as a consultant paediatrician at The University Hospital of North Durham, County Durham, Dr Speight is the best ME children's consultant in the UK.

**Professor Martin Pall**

**Professor of Biochemistry and Basic Medical Sciences,
Washington State University USA**

Professor Pall has long-term interests in biological regulatory mechanisms. His current research is focussed on a theory he has developed on the cause (etiology) of chronic fatigue syndrome and the overlapping and related conditions of multiple chemical sensitivity, fibromyalgia, and posttraumatic stress disorder. According to this theory, each of these is initiated by stresses that induce increased levels of nitric oxide and its oxidant product peroxynitrite, followed by a biochemical vicious cycle mechanism associated with chronic elevation of these two compounds. Symptoms of these conditions are produced by both nitric oxide and peroxynitrite and treatment should focus on downregulating this vicious cycle mechanism. Vitamin B-12 injections commonly used to treat these conditions are proposed to act through the action of one form of B-12 (hydroxocobalamin) which is a potent nitric oxide scavenger. Dozens of biochemical and physiological observations provide support for this theory. The most puzzling features of these conditions are explained by this novel theory.

ME News from Around Europe

Invest in ME believe that the seriousness and the scale of myalgic encephalomyelitis requires an international focus and this requires scientists, researchers, healthcare professionals and ME Support groups in all countries to work together. Collaboration may be the key to success and this means taking a consistent approach to research, diagnosis and treatment. The following updates from around Europe and USA were some of those Invest in ME received for the conference from people working in the ME community in other countries and illustrate the current status and problems in these countries.

Norway – A Breakthrough?

Recent news from Norway gives hope that changes are afoot in the way myalgic encephalomyelitis is being perceived and treated. After much campaigning the results of the Norwegian ME-forening (the Norwegian ME Association - the main support group for people with ME in Norway) is bearing rewards.

On Thursday 29th March Stortinget (Norwegian Parliament) completed a 1 hour and 10 min debate about ME and what should be done about the situation. This has led to the Norwegian Minister for Health and Care Services announcing publicly a long list of proposals which she stated will be put into action to ensure that ME-patients get proper care. The minister, Sylvia Brustad, has now engaged herself personally in the case of ME. The health minister is on record as stating that more knowledge, support, research and funding is required to provide an adequate approach to this illness which is estimated to affect 10,000 Norwegians.

"This is an illness which is difficult to diagnose and treat, and it is an illness to which health services have, up till now, given too little attention. This the government will change, and we will follow this up in the budget process" said minister Brustad.

Severe ME - A story from Norway

The story of the Krisner family from Norway was shown on the Invest in ME Conference DVD from 2006 – a story of one family where three siblings severely affected by ME. The mother, Kjersti, is a brave, resourceful and inspirational woman who manages still to see positives from the terrible situation. For those who have not seen the Norwegian TV channel Puls' film please go to –

<http://www.investinme.org/Mediatelevision3.htm>

We called Kjersti to ask her how things were a year on. Her children are still very ill. Katrine, 28 years old in May, has been ill since the age of 20. She is the worst affected. She cannot communicate at all and touching her even gently hurts. She is being tube fed and in nappies. There are moments of hope but they are very tiny and don't last long – sometimes a smile or being able to hold her mother's hand. Once her mother was able to give her a hug.

Bjornar, 30, is still lying in total darkness but can talk a little bit in the afternoon. He is getting mentally stronger and wants so much to get out of his situation but the body is too weak. The family can't see him because he cannot tolerate any light and his room has to be kept in total darkness.

Frode, 20, can get out in an electric wheelchair and work on a computer a couple of hours a day. He has started an internet company and is stable as he knows his limits.

The Krisner family now have help in the form of a community nurse who comes and helps in the daytime. Before, the family had to manage all the care themselves and that has meant that Kjersti hasn't been able to sleep much for many years as the children are so severely affected and have all different sleep patterns. Kjersti is optimistic and despite everything they laugh a lot in the family and she is constantly helping others in a similar situation. She is collating information on people with M.E. in Norway who are bedbound and who are tube fed. She says it is easier to do that in a small country and it gives vital information for the politicians. Kjersti feels patients themselves, and carers, are the experts in this illness and should be listened to. She wished us well with the conference and would have liked to attend but obviously she can't - but said she believes one day her turn will come.

Such a strong and inspiring family despite everything.

Denmark

The situation for ME/CFS patients in Denmark is deplorable. Although the disease is officially accepted as a physical one, the health care community and the media treat it like a psychological one. There are no government-appointed specialists and there are very few doctors who believe the disease is real. Of these very few, we know for sure that two have been told by their hospital supervisors that they may no longer treat "that type of patient." Given this environment, very few doctors dare to give the G93.3 diagnosis. Some patients have been forced to accept a F48 diagnosis in spite of the fact that no psychological illness was found just to get a much-needed pension. Needless to say, there are no hospitals or clinics that treat or monitor the disease.

Only one study has ever been done about ME/CFS in Denmark: "Illness and disability in Danish CFS patients at diagnosis and 5-year follow-up" by Andersen, Permin and Albrecht. The 9-year follow-up paper is soon to be published. It is an important study, because it shows that "recovery and substantial improvement are uncommon" – around 6% - and that "good mental health does not predict improvement." So although the patient's mood improved over time as they learned to cope with their illness, their physical symptoms worsened. This should give the pushers of CBT-as-cure something to think about!

Overall, ME/CFS patients in Denmark are horribly neglected and many have given up hope of ever being taken seriously by the Danish health care system. The hope of the Danish ME/CFS Association is that we can soon bring about change like that which has recently been seen in Norway

- Rebecca Hansen Consultant /Danish ME/CFS Association

Spain

Dear friends and colleagues far and near,
Yesterday, the Catalan Parliament accepted the Popular Legislative Initiative on Chronic Fatigue Syndrome/ME and Fibromyalgia (FM), presented by representatives from 80% of the people with CFS/ME or FM who are in associations in Catalonia.

This acceptance is the first step towards a world-first:

a law that would ensure proper services for people with CFS/ME and FM and a fair treatment by medical inspectors.

No one thought that a group of ill people like us, in a not so user-friendly country would be able to pull this off. So we are all very happy and it is a big boost for the CFS/ME and FM community here.

Now that it has been accepted, the signature gathering can begin. We need 50,000 signatures and we have a team of 150 signature-collection coordinators ("fedetarios") ready to roll. Once the signatures are gathered, the law will be discussed in parliament and voted. This will probably take place in the fall.

Up to now, it has been a lot of work for us sick folks: writing the law and the document to justify each article of the law (thank you to all of you who sent me the necessary bibliography!), working with all the associations to create unity and the much needed empowerment, meeting with all political groups and sub groups (we have the support of all the political parties, except, of course, the party that runs the Health Ministry), campaigning to recruit signature coordinators, meetings with unions, women's groups others.

It has not been easy as we are presenting a proposed law that puts totally into question the government's plan to keep CFS/ME and FM solely in Primary Health Care (where most doctors do not believe these illnesses exist or do not want to work with them and are not allowed to do any relevant tests), while our law, amongst other things, demands CFS-FM units. So we have had (and continue) to deal with pressures, intimidations, etc, from government and government-related organizations. We are also having to deal with the two foundations (one run by the government party, the other run by businessmen) who, up to now, had managed to control and manipulate the CFS and FM associations in Catalonia and create division.

Encouraging the associations to be independent and to create unity has been hard but the most rewarding work. The documents (the law, the justification document and other documents) are available in Catalan and some in Spanish. If anyone is interested in receiving them, let us know.

-Clara Valverde (Promoting Commission of the CFS/ME-FM Popular Legislative Initiative, Catalonia, Spain)

ME News from Around Europe (*continued*)

Germany the sick man of Europe?

Wasn't that a headline of "The Economist" some years ago? Referring to the economic situation the magazine certainly didn't think of the situation of people with ME/CFS in Germany. Though there's said to be a slight upswing now, "The Economist's" description still applies to the health care provisions for people with ME/CFS. They are more or less non-existent. Germany is – compared to the UK – indeed the sick man of Europe.

From our point of view the establishment of 50 CNCCs and LMDTs for England alone is a great success. The public awareness seems to be much more advanced than over here. We admire your determination, resilience and efficiency by which you have achieved this.

From our point of view all that is the result of years of tenacious work of hundreds of active people who did not allow themselves to be deterred by all the obstacles they met on their way to a better care for people with ME/CFS. In a way you are our great role model when it comes to the situation of people with ME/CFS – in spite of all shortcomings and tragic cases like that of Sophia Mirza and others who died or are treated badly.

Here in Germany the situation is by far not as advanced. There isn't a single clinic which is specialised in ME/CFS. People are more or less left on their own and depend on their GPs. Only a handful of physicians are interested in the subject and care for people with ME/CFS, among them unfortunately also some quacks and cutthroats. Those who do serious work keep themselves in the hiding because otherwise they would be swamped with desperate and extremely needy people, searching for help and support.

However, the patients sometimes have GPs who are sympathetic and willing to support them though their knowledge of ME/CFS mostly is quite limited. The physicians themselves are in a fix because there is no structure like a CFS society for physicians, no advanced training or other provisions where they can get information. Open-minded GPs read the information which is distributed via the national charity Fatigatio or websites like www.cfs-aktuell.de or www.cfs-portal.de.

Thus the majority of the 250.000 or 300.000 sufferers in Germany do not even have a diagnosis. Those who suspect having ME/CFS or whose GPs assume this might be the case don't have a place where to go and confirm or exclude the diagnosis. There is no place where they can get a proper advice in medical, social or legal matters. Most people have difficulties to get incapacity benefits on the basis of having ME/CFS. Yet this is not a "recognised" diagnosis but things are gradually changing.

The vast majority of sufferers still end up in a psychiatric ward or in the practice of a psychologist or psychiatrist – getting a psychological or psychiatric "diagnosis". More often than not incapacity benefits are paid on grounds of such a diagnosis and people often accept it with resistance because they have no choice. The psychosomatic health care provisions in Germany are quite good and they serve as some kind of waste disposal for all diseases which the physicians are not familiar with or cannot diagnose. Small wonder, that almost all ME/CFS patients are given a psychiatric diagnosis, leaving them in an even more desperate situation. They are told they'd have a depression, a psychosomatic or somatoform disorder (meaning it only looks like a somatic disease but in reality is all in the mind), a minor and insignificant functional disease.

In Germany ME/CFS is mostly considered to be a functional somatic syndrome, i.e. a more or less psychiatric disease. Only recently (in February 2007) some psychiatrists published an article in "The Lancet" titled "Management of functional somatic syndromes" (by Peter Henningsen, Stephan Zipfel, Wolfgang Herzog), in which the biomedical research is completely ignored.

There is one national charity for people with Me/CFS founded in 1993 with the name "Fatigatio e.V.". Of course, the few people who run the charity cannot come up with the demand. The charity does not have the necessary resources, neither financially nor personally. There are also some local self-help groups, however, with little influence on the overall situation. Yet, there are more and more physicians who say "Oh yes, I've heard about this," and who take matters seriously.

(Continued on page 37)

ME in Germany – continued from page 36)

After all, campaigns like SPARK in the USA and the good work that is done in Great Britain and all over the world has some trickle down effect.

Looking to the UK and your achievements provides us hope and confidence that we will one day no longer be forced to living in the sticks. All in all you can see that we in Germany are lagging behind your developments at least 15 or 20 years!

By Regina Clos

Regina Clos has worked for some years for the national charity Fatigatio and is now running a German spoken website (www.cfs-aktuell.de) with up-to-date information on ME/CFS and many translations of articles and booklets published in Great Britain, Australia, the USA and Canada. She is a sufferer herself for more than 20 years and became a translator after she had to give up her job as a teacher for handicapped children.

Sweden

In Sweden, ME is largely unknown by doctors as well as the general public. To the extent it is discussed, it is under the name of "Kroniskt trötthetssyndrom", which literally translates as "Chronic tiredness (not fatigue!) syndrome".

There are no ME specialists available for diagnostic evaluation or treatment management. The ME clinic at Huddinge Hospital in Stockholm was closed in 2000. Some patients have been diagnosed at the Gottfries Clinic in Gothenburg which specializes in Fibromyalgia and CFS, but getting a referral can be difficult or impossible depending on where in the country you live. This clinic is also under the threat of losing public funding and being forced to close down.

There are a few individual doctors with some knowledge of ME, and some GPs who are willing to learn, but for the most part patients are left to GPs that range from ignorant to downright insulting. The view that all forms of chronic fatigue equal a somatoform syndrome is widespread, and reinforced through articles in the medical union's member journal, "Läkartidningen".

We believe ME is tremendously under diagnosed in Sweden. The code G93.3 is virtually never used, and patients with this diagnosis code may have it changed by a new doctor without explanation. Most likely, sufferers are instead diagnosed with "burn-out syndrome" (or "exhaustion depression"), as this was a very common problem in Sweden particularly during

the 1990's. The obvious problem with this misdiagnosis is that it leads to unreasonable expectations on recovery speed and capacity for physical activity. With time, when the patients don't improve and claim to be unable to exercise, they are met with increasing disbelief from doctors and others.

There is also a strong tendency in Sweden at the moment to question the "overuse" of sickness benefits and reduce the number of claimants by rejecting more claims. As in many other countries, special insurance doctors second-guess the patient's own doctor, and some claim illnesses such as ME and Fibromyalgia don't exist. This puts many patients in a desperate financial situation. Some fall between the chairs when they are considered too healthy for sickness benefits, but too sick to register as unemployed and claim unemployment benefits.

The research being carried out has mostly focussed on the psychosomatic angle, and included larger groups of chronically tired patients who do not fulfil stricter ME criteria.

However, Professor Gottfries and his colleagues in Gothenburg have conducted a very promising trial using a staphylococcus vaccine. 2/3 of patients experienced positive effects, especially on immune symptoms and recurring infections. Many were able to return to work or increase the number of hours worked, and generally increase their quality of life. Unfortunately, this research has now been stopped due to manufacturing problems with the vaccine, and patients doing well on the treatment for several years are being forced back to a life of illness as the supplies run out.

The national patients' organisation, RME, has approximately 370 members, and is working with very limited resources to improve the situation for sufferers and increase awareness. Some regional groups have been making limited progress, but it's very much a process of one step forward and two steps back.

Anna Fenander, RME Stockholm

Facts About ME

ME is now 5 times more prevalent in the UK than is HIV/AIDS.

ME News from USA – Pat Fero – Wisconsin ME Group

Investing in ME...from the other side of the pond

By Pat Fero, MEPD

I live in Wisconsin, which is the other side of the pond, and a few Great Lakes over to the Midwest, USA. It is only through information technology that I know about Myalgic Encephalomyelitis in 2007.

When I first saw the words Myalgic Encephalomyelitis, I did not search with fervor to synthesize medical information into my growing understanding of CFS issues. Despite working as Executive Director of the WISCONSIN CFS ASSOCIATION and being on the Board serving in one capacity or another since 1987, it was 2003 or 2004 before I began to look at ME. Why is that? This is the landscape question, the backdrop for what follows, that is, my perceptions about ME and about CFS in the United States.

Humans learn best when they have a need to know about a thing. When that happens they are ready to ask questions. Here in US, the need to know about ME exists with a few vocal advocates and people who have quietly investigated ME for the sake of "name change." Within that group, controversy rages, but that is the only place CFS diagnosed patients give ME an iota of thought. Why is that?

First, I believe that in the United States, with about 300 million people and a land area of over 9 million square kilometers, we do not have a CFS community. To foster community development that would create a shared understanding of CFS would mean organized education, awareness and advocacy. If we had a community, the vast numbers of diagnosed CFS patients would be far greater than a mere 20% of an estimated 800,000.

By far, the majority of people ill have no diagnosis or are misdiagnosed. That being the case, MD's and other medical professionals have little need to know about CFS and the few of us presenting in the doctors offices can easily be disregarded. In fact, sweeping CFS into a larger entity of fatigue and pain is the logical outcome. Investing in research centers to study pain mechanisms and fatiguing illnesses, denies the integrity of CFS.

Integrity? Historically, ME has integrity as a distinct illness entity with diagnostic criteria until issues

muddled when the US became involved with international researchers and MDs. THIS is a generalization and an oversimplification. However, we can cite the mid 1950's work of Melvin Ramsey and John Richardson. In contrast, looking for integrity in CFS as a distinct illness entity with diagnostic criteria is impossible. I agree with Dr. Byron Hyde that once the Centers for Disease Control became involved in the Lake Tahoe epidemic, outbreak, incident and finally non entity, patients in the US suffering from ME, were left to wander about until the powers that be met in 1988 to label their illness chronic fatigue syndrome.

In 1988, where I live, there was integrity in CFS. By this, I mean that my communications were with 100's of people who had like illness experiences. 5 years and many 100's of calls later, I knew that the "CFS" experience changed. Much later, I found that my perceptions were correct. The CFS pain and fatigue waste bin was huge as was my familiarity with lists of co morbid psychiatric conditions that I had never heard of until the mid 90's.

In 2000, in WISCONSIN, our CFS organization decided that our mission of education and awareness was too narrow. What was the topic? How could we sort out this waste bin of misdiagnosis, over diagnosis and under diagnosis? What a mess.

On a national level with a small group of people compared to the potential whole, we are a huge dysfunctional family. Bitter, personal infighting over tiny issues signals the loss of hope to stop the CFS non-entity spiral.

I see ways to stop enabling and perpetuating chaos.

In the US, first, we must work on developing CFS community. This means a massive information campaign in 52 states. Because our public health institutions are in the middle of the Chaos, the effort has to start grassroots from people like me and the wonderful people in Atlanta and Northern Virginia and Vermont and Chicago and...and. We cannot forget about the people in Wyoming or Montana or anywhere else where the population density is so low that we might think that sick people do not count.

Secondly, I believe that existing US national, state organizations and regional groups must be inclusive to promote collaborative efforts that will stop sick people from reinventing the wheel.

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(News from USA – continued from page 38)

It is a waste time and energy. In addition, we have wonderful independent groups in the US totally devoted to ME. Those involved are sick, they are dedicated and they work. YES!

A continuum of thought is as real as the color wheel. Do we say... pink is not a primary color.... OOPS...not allowed? What about sky blue pink? You know exactly what I mean and whatever mind image you have of sky blue pink, that hue (s) is not on the color wheel at all.

I don't know how to promote collaborative efforts other than narrow the focus to the basis for all like human endeavors: people in need, really sick people with fractured families, some on the streets need information and help. Many kind people here with CFS work on this every day. We just need a more organized effort and to find ways to help them help others.

Thirdly, Chaos creates phantom enemies and it is easy enough for an institution and people to obstruct progress by perpetuating the same old stories. Are there real enemies?

I think a combination of factors makes people behave badly and as a result; whole groups suffer with no understanding, let alone help.

In addition, people interested in power and establishing an identity through CFS advocacy or CFS research perpetuate chaos because they tend to be exclusive.

My thought would be to ignore anyone who would obstruct by deceit, hostility and engaging in activities to merit a few, not the whole. I would seek out the 100's of people working for the common good and forget the rest.

I am investing in ME by tackling problems in my own back yard. I have to work with what is and we have a long way to go before my ME will be recognized or diagnosed in the United States.

I am Investing in ME. The founders, in the right place, at the right time, are bringing order from chaos. What a wonder it has been to watch from afar!

HELLO from WISCONSIN and THANK YOU!

Story – A Carer of a Person with ME

By Greg Crowhurst

Caring for someone with severe ME - Five Stark Facts

There is no support, there is no cure, there is no treatment, there is no government funded physical research and there is little truth in any of the official policy statements.

The scale of the suffering is off the scale. The severely affected will experience not a moment's relief, often for decades on end. Sufferer and carer are routinely pushed to the limits of human endurance.

The severely affected are likely to be experiencing between twenty and thirty intolerable symptoms all at once. This includes pain, paralysis, numbness, sickness, unbearable hypersensitivity and incredible physical disability.

Fatigue is not the issue; it is only one symptom among many; Post Exertional Malaise is the major concern. Any exertion is likely to have a shocking after-effect, typically 24 to 48 hours afterwards, which can lead to days, weeks, years of worse symptoms or even death.

Sufferer's and carer's are unwilling pawns in a political game. There is overwhelming evidence of powerful vested financial interests at work, across all levels of government, trying to suppress the physical reality of ME, which is far more prevalent than AIDS or MS. Currently, the main interventions on offer are psychiatric.

ME Story

My GP thought I had ME but kept saying, work through it, do lots of exercise you'll get over it. They sent me to a sports centre to do a fitness course but I went once and never again. It was about this time I saw the psych and he said there was nothing mentally wrong that feeling well again wouldn't fix - Jas

NICE - liME Response to Draft Guidelines on ME

The National Institute for Health and Clinical Excellence (NICE) have recently published their draft document for clinical guidelines. The document is being developed for use in the NHS in England and Wales regarding chronic fatigue syndrome / Myalgic Encephalomyelitis (CFS/ME).

Although not an original stakeholder (liME only became a charity in May 2006) we have nevertheless registered to become a stakeholder in these guidelines and have supplied our response directly to NICE.

Our full response is available here –

www.investinme.org/Documents/PDFdocuments/Invest%20in%20ME%20Response%20to%20NICE%20Draft%20Guidelines.pdf

Summary of Response from liME:

The reaction to the NICE guidelines can be summed up as profound disappointment that NICE have chosen to highlight, yet again, Cognitive Behavioural Therapy (CBT) and Graded Exercise (GET) as the most effective forms of management (aka treatment) for ME.

Psychiatric paradigms are referred to and recommended as therapies and as treatments for ME despite ME patients and groups stating they are ineffective or harmful.

Graded Exercise Treatment (GET), already known to be potentially harmful to people with ME, is put forward as a therapy/treatment

GET is put forward, along with Cognitive Behaviour Therapy (CBT), as treatments of first choice

The NICE group formulating these guidelines show a disingenuous side by comparing the use of these treatments for ME with the use of these treatments for cancer and diabetes and other illnesses. Yet CBT is not offered as first line treatments for these illnesses which NICE are recommending here for CFS/ME.

It is not for sensation that liME would like to see a lawyer added to the NICE consultation group. The lawyer would be there to represent ME patients as one can foresee that there will be litigation against the people making recommendations for use of GET/CBT when a patient suffers, or dies, from putting into practice such guidelines.

liME believe these Draft Guidelines should state unequivocally that it is unacceptable for patients with ME to be subjected to "sectioning" by psychiatrists, supported by Social Services and the Police, simply because the person has ME.

We dispute the frequent statements characterised by this text 'There is little understanding of the nature of the disease '. There are over 4000 biomedical research papers on the illness which the NICE searches should have seen and analysed.

The NICE guidelines do not carry a single reference to the relationship between vaccinations or epidemics.

The document is inconsistent in a number of areas - especially terminology.

The inclusion of as wide a possible base of chronic fatigue states in the draft guidelines is clearly evidenced and does a disservice to pwme

Essential biomedical research which distinctly shows the biological nature of ME is ignored

The lack of proper discussion of the Canadian guidelines shows not only a bias to outdated and flawed information but invalidates much of the data used to justify the proposals

The layout and format of the document is poor.

The objectives of the Nice Draft Guidelines are not met.

The credibility of NICE is now severely compromised.

Yet again ME patients seem to be on the receiving end of another counter-productive and biased analysis. The document shows little new thinking and is clearly lacking in impartial analysis of all areas of research into ME.

*Both the Chairman and CEO
of NICE were invited to speak
at the conference but both
declined*

The Gibson Inquiry

"This group believes that the MRC should be more open-minded in their evaluation of proposals for biomedical research into CFS/ME and that, in order to overcome the perception of bias in their decisions, they should assign at least an equivalent amount of funding (£11 million) to biomedical research as they have done to psychosocial research. It can no longer be left in a state of flux and these patients or potential patients should expect a resolution of the problems which only an intense research programme can help resolve. It is an illness whose time has certainly come."

Thus concluded the report from Dr Ian Gibson (MP)'s Group on Scientific Research in to Myalgic Encephalomyelitis (ME) – otherwise known as the Gibson Inquiry. Unfortunately, that time is too late for some of the victims who have lost their lives to this devastating illness.

Invest in ME welcomed the broad message of this report when it was published in November 2006. The Inquiry called for ME to be given due recognition, alongside heart disease and cancer. It also called for ring-fenced money for bio-medical research as happened with AIDS. ME in fact affects five times as many people as does AIDS in the UK but can have a much more devastating impact on quality of life. The Inquiry recommended that research must be made a priority and suggested that £11 million should be made available for research to redress the balance in an illness where too much emphasis had been put on psychological "coping strategies". The Inquiry accused the MRC of merely "paying lip-service" to the call for bio-medical research.

Invest in ME felt that at last an official acknowledgment was given that ME is a severe, incapacitating, illness and that those who suffer from it, as well as their carers and families, may have their lives completely ruined. Invest in ME have been asking for a long time for very simple, common-sense things such as the adoption of comprehensive diagnostic criteria and epidemiological studies. We were delighted that the report agreed that this was vitally important.

This report did not stint in its criticism of the Medical Research Council and NICE. Indeed, it warns that NICE should rethink very carefully one of its recommended treatments, Graded Exercise Therapy (GET), because of evidence that in 80% of M./E. sufferers there was diastolic cardiomyopathy. Invest in ME has warned NICE during our review of the Draft NICE Guidelines for ME that by recommending GET they would put patients lives at risk, and risk Judicial

Review. We still hope that NICE will take notice. Invest in ME also welcomed the call for an independent scientific committee to be established to oversee all aspects of research, as well as an inquiry into the vested interests of insurance companies whose advisors also act as advisors to the DWP. Dr Gibson's Group recommended an investigation of these vested interests by a standards committee because, it stated, too often patients have to live with the double burden of fighting for both their health and their benefits.

Invest in ME believe that we must use the positive aspects of the inquiry report and move forward and ensure that people are correctly diagnosed with this illness and that doctors and scientists treat patients knowing and accepting that they have a genuine and serious illness.

Invest in ME have called on the government and MRC take this opportunity and work with the ME community and biomedical researchers to ensure that this illness can be understood, that proper biomedical research is funded and that archaic and unjust perceptions by government departments, sections of the health service and those responsible for deciding funding strategy are once and for all discarded.

Dr. Gibson has created an opportunity to benefit patients and find a cure for this illness. Invest in ME ask the government to ensure that this opportunity is not lost and that yet another generation of UK citizens is not abandoned. Full report available at - <http://tinyurl.com/ynqhtc>

IiME's reactions to the report are at -

<http://tinyurl.com/2aqnye>

ME Story

We arrived at the doctors and the female doctor refused to see me, saying I was not her patient, and she wasn't prepared to see me. I was just in a state of shock and my partner was furious. The Doctor in question didn't come out to the waiting room to see me, instead wrote a prescription for three months of anti-depressants - Jan

INFORMATION ON ME/CFS

by Margaret Williams

(updated) April 2007

ME/CFS is a complex, whole body systemic disorder and it is difficult to compile a unified reference list of the documented biomedical abnormalities, since so many medical disciplines are involved (eg. musculo-skeletal, immunological, neurological, endocrinological, gastro-intestinal, ocular, cardiovascular, respiratory etc). The reference papers themselves overlap considerably.

The biomedical reference papers now number over 4,000 and some of these reference papers are listed in 92 pages of references online at http://www.meactionuk.org.uk/SUBJECT_INDEX.htm.

The few illustrations below provide indisputable evidence of organic disease, thereby demolishing the psychiatric lobby's assertions that there is no such evidence.

The reference papers can be broadly categorised into the following sections and it is necessary to be familiar with all sections.

HISTORICAL PAPERS ON ME

These date from 1957 -- 1980 and include excellent clinical descriptions, laboratory-determined abnormalities and post-mortem findings.

GENERAL PAPERS ON ME/CFS

These papers cover more than one aspect of ME/CFS and include for example evidence of impaired oxygen delivery to muscle; evidence of delayed recovery from fatiguing exercise and documented symptoms commonly found in ME/CFS (which number over 60).

LABORATORY FINDINGS IN ME/CFS

Although there is as yet no single, specific, definitive test for ME/CFS (which is also the case in numerous other medical conditions including multiple sclerosis), nevertheless there is an entirely consistent and reproducible pattern of laboratory-determined abnormalities which have been observed and documented worldwide. Such abnormalities particularly include dysfunction of immunological, neurological, neuro-endocrinological, musculo-skeletal, cardiovascular, pulmonary and cognitive parameters.

QUALITY OF LIFE IN ME/CFS

One international ME/CFS expert writes that in his experience, ME/CFS **"is one of the most disabling diseases that I care for, far exceeding HIV disease except for the terminal stages"**. Australian research describes ME/CFS patients as suffering more dysfunction than multiple sclerosis sufferers; the sickness impact profile (SIP) is more extreme than in end-stage renal disease and heart disease, and only in terminally ill cancer patients has the overall SIP score been found to reach that found in ME/CFS. American research found that the quality of life in patients with ME/CFS is significantly, particularly and uniquely disrupted, and that the illness causes marked disruption and devastation. Scandinavian research has shown that patients with "non-visible" disability suffer more stigmatisation than those with visible disability.

CHRONICITY AND SEVERITY OF ME/CFS

This section provides evidence of the natural history of severe ME/CFS, showing that the prognosis is extremely poor for the severely ill subset, with no symptom improvement (only 4% recovered) and it shows symptom patterns in long-duration ME/CFS.

PRECIPITATING FACTORS IN ME/CFS

The syndrome is known to be related to a dysfunctional stress response, and there is evidence that precipitating factors include physical trauma (specifically a breakdown in the blood-brain barrier) and critical life events. Other factors include infections; anaesthesia; immunisations and exposure to certain chemicals.

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INFORMATION ON ME/CFS (*continued*)

EPIDEMIOLOGY OF ME/CFS

Various papers on the epidemiology of ME/CFS reveal that considerable misinformation exists regarding the appropriate evaluation of ME/CFS (including age, gender, occupation, geographical location, length and severity of illness) but that there is increasing understanding of the prevalence, incidence, risk factors, illness patterns and prognosis of this complex multi-system disorder, and emphasis is placed on the importance of subgroups. Although ME/CFS is one of the commonest chronic neurological conditions in the UK today, no official government-sponsored statistical evaluation has yet been made, possibly due to the heterogeneity of the disorder and the lack of a concise case definition.

NEUROENDOCRINE ABNORMALITIES IN ME/CFS

This section shows evidence for and implications of the endocrine disruption found in ME/CFS, especially that associated with hypothalamic-pituitary-adrenal axis dysfunction. CT scans of the adrenal glands have revealed that both the right and left adrenal glands of some ME/CFS patients are reduced in size by 50% when compared with healthy controls.

NEUROLOGICAL ABNORMALITIES IN ME/CFS (including vertigo and seizures)

These papers show commonly found dysfunction in both the central nervous system and in the autonomic nervous system; they include papers on dysequilibrium and vertigo which are known components of severe ME/CFS, and there is evidence that seizures may occur in ME/CFS.

DEMYELINATION IN ME/CFS

Evidence of demyelination and cerebral oedema has been documented in the ME /CFS literature since 1988.

OCULAR PROBLEMS IN ME/CFS

There is evidence that such problems include intermittent jelly-like nystagmus; difficulty in accommodation / focusing / visual acuities; photosensitivity; photophobia; blurred vision; double vision; crusted eyes; dry eyes; itchiness; narrowed arterioles; retinal defects; fibrillar changes in vitreous; chorioretinal macular abnormalities and optic pallor (the latter is also observed in MS). Objective findings of the anterior segment suggest an organic aetiology.

LIVER / SPLEEN INVOLVEMENT IN ME/CFS

Published evidence shows that enlargement of the spleen and liver is not unusual. Evidence shows infiltration of the splenic sinuses by atypical lymphoid cells, with reduction in white pulp, suggesting a chronic inflammatory process.

HAIR LOSS IN ME/CFS

Hair loss in ME/CFS is documented in the literature. One author states **"It is a rare woman with CFS who has not had hair loss, usually diffuse and non-scarring"**. Elsewhere, it is documented as occurring in 20% of patients.

MOUTH ULCERS IN ME/CFS

Mouth ulcers have been documented in the ME literature since 1955.

VIROLOGY IN ME/CFS

Evidence reveals the known tropism of Coxsackie B viruses for muscle, brain, heart and pancreas, all of which are documented as being target organs in ME. There is also evidence of human herpes virus 6 (HHV6) reactivation playing a role in the pathogenesis of both ME/CFS and MS. HHV6 Variant A is more common in AIDS and ME/CFS, whilst Variant B is found in MS. HHV6 used to be called human B-lymphotropic virus (HBLV); it was discovered in 1986. It is possible that reactivation of a composite viral load occurs as an epiphenomenon of an underlying immune system dysfunction, thus giving rise to the protean symptomatology.

(continued on page 44)

INFORMATION ON ME/CFS (*continued*)

OVERLAP OF ME/CFS WITH POST POLIO SYNDROME

Prestigious papers, for example, Annals of the New York Academy of Sciences 1995 (containing 50 papers on clinical neurology, neuroscience, electrophysiology, brain imaging, histology, virology, immunology, epidemiology, with contributors from the US, Australia, Canada, France, Sweden and the UK) point out the similarities between post-polio syndrome and ME/CFS, notably that the mechanism of the extreme fatigue (called "visceral exhaustion") -- is exactly the same in ME/CFS as in PPS.

STRESS ENHANCES SUSCEPTIBILITY TO INFECTION

There is substantial evidence that concurrent stress at the time of viral exposure leads to more severe disease. Stress is known to increase susceptibility to those diseases that are immune-related, eg. infectious disease, cancer and autoimmune disorders.

PSYCHONEUROIMMUNOLOGY

There is a vast literature (from 1884 to date) on the pathway of causation whereby stress, especially traumatic stress, affects the immune system and potentiates disease development.

CHEMICAL INJURY TO THE BLOOD BRAIN BARRIER

There is published evidence to show that one mechanism of causation is likely to be a combination of stress and chemicals, resulting in chemical trauma to the brain via a breaching of the blood brain barrier (BBB): stress can intensify the effects of some chemicals, making them very harmful to the brain, nervous system, and liver (resulting in congested blood vessels, reduction of an important enzyme and abnormal fatty deposits), leading to cellular death, especially when chemicals are combined. The ability of chemicals to leak from one area of the brain to another holds the potential for much greater damage to occur in the entire brain.

IMMUNOLOGY IN ME/CFS

The most commonly found immune abnormalities are very low natural killer (NK) cells, with decreased cytolytic activity, and an increased CD4 - CD8 ratio; there is an increase in the CD8+ cytotoxic T cells bearing antigenic markers of activation on their cell surface; there are higher frequencies of low levels of various autoantibodies, especially anti-nuclear and anti-smooth muscle antibodies; there are low levels of circulating immune complexes; there are increased levels of IgE and decreased levels of IgG3. Low levels of IgG3 have been reported since 1986 in patients with aching muscles. Overall, these abnormalities are consistent with evidence demonstrating chronic, low-grade immune activation in ME/CFS. In 1994, an international ME /CFS expert (Dr Paul Levine of the Viral Epidemiology Branch of the National Cancer Institute, Bethesda, Maryland) stated " the spectrum of illnesses associated with a dysregulated immune system must now include CFS" (*ref: Clin Inf Dis 1994:18 (Suppl 1):S57-S60*). Importantly, it has been convincingly demonstrated that changes in different immune parameters correlate with particular aspects of disease symptomatology and severity.

ALLERGIES and MULTIPLE CHEMICAL SENSITIVITY (MCS) IN ME/CFS

The relationship between viral infections and onset of allergic disease is well-documented in the medical literature. With specific relationship to ME/CFS, there is overwhelming published evidence that allergies, food intolerance and multiple chemical sensitivities (MCS) are very common; an increasing sensitivity and adverse reaction to many drugs / therapeutic substances is widely believed to be virtually pathognomonic of ME/CFS. Cells cannot be attacked by the immune system unless they display on their surfaces complex glycoprotein molecules known as Class II MHC antigens; cells can be induced to do this by gamma-interferon, which is an anti-viral chemical produced by the immune system when under viral attack. Allergies in ME/CFS are thought to be the result of this mechanism, which makes the body cells susceptible to on-going attack by the immune system. Because reference to allergies is so widespread throughout the ME/CFS literature, many of these references are to be found throughout the reference papers, mostly in the sections on General ME /CFS, Immunology, and Neuroendocrinology. More and more patients are presenting with "total allergy syndrome"; this is recognised as part of ME/CFS; whilst some psychiatrists are notoriously dismissive about its existence, the literature (from highly reputable internationally acclaimed experts) clearly shows that it does exist, and that such patients do indeed develop abnormal immune parameters whilst under observation.

(continued on page 45)

INFORMATION ON ME/CFS (*continued*)

A leading professor of clinical immunology in the UK has published papers confirming that these are patients with multiple sensitivities, and that their symptoms are not all in the mind.

ANAESTHESIA PROBLEMS IN ME/CFS

It is well-established that patients with ME/CFS and others with neuromuscular dysfunction can have problems with anaesthesia: depolarising muscle relaxants have a known risk of causing potassium release from muscle, which can lead to cardiac arrest, and it is important to avoid histamine releasers. Muscle weakness increases the risk of respiratory failure.

VASCULAR PROBLEMS IN ME/CFS

References to vascular problems in ME/CFS have been in the medical literature from 1938. Such problems include vasomotor instability; impaired blood flow in the micro-circulation consistent with inflammatory processes; vasculopathy including Raynaud's disease; cutaneous vasculitis; vasculitis of the liver and cerebral hypoperfusion due to vasculitis.

CARDIAC PROBLEMS IN ME/CFS

Documented problems include myocarditis; chronic pericarditis; paroxysmal attacks of chest pain, with the intensity of myocardial infarction; palpitations, with sinus tachycardia being particularly troublesome; flattening and inversion of T waves; a lower stroke volume and cardiac output (indicating a defect in the higher cortical modulation of cardiovascular autonomic control). ME/CFS patients have higher heart rates and lower pulse pressure and have baseline differences from normals.

LUNG / RESPIRATORY PROBLEMS IN ME/CFS

There is evidence of shortness of breath in ME/CFS patients (due in part to fatigue of the voluntary muscles of respiration); evidence shows that ME/CFS patients have a significant decrease in vital capacity (VC). The incidence of bronchial hyper-responsiveness is remarkably high. Compared with controls, ME/CFS patients showed a significant reduction in all lung function parameters studied.

GUT DYSFUNCTION IN ME/CFS

Irritable bowel syndrome (IBS) is a widespread and common problem in ME/CFS; reference to it is to be found throughout various sections of the reference papers.

BRAIN IMAGING (NUCLEAR MEDICINE) IN ME/CFS

The literature contains objective evidence of brain impairment in the majority of patients which is compatible with a chronic viral encephalitis. Patients have a particular pattern of hypoperfusion of the brainstem. Brain perfusion impairment in ME/CFS provides objective evidence of central nervous system dysfunction.

COGNITIVE DYSFUNCTION IN ME/CFS

Neuropsychological testing reveals a pattern of cognitive impairment which is compatible with an organic brain lesion. Tests on ME/CFS patients revealed a performance which was sevenfold worse than that found in either the controls or in depressed patients. Results indicate that the memory deficit in ME/CFS is more severe than has been assumed by the CDC criteria. A pattern has emerged of brain behaviour which supports neurological compromise in ME /CFS.

PSYCHOLOGICAL PROBLEMS IN ME/CFS

There is a substantial body of literature which strongly refutes claims that patients are overly suggestible; it is quite specific that patients are not somatising, and it confirms that patients are not exhibiting "abnormal illness behaviour" and that the illness is not explained by inactivity or psychiatric disorder. Any depressive symptoms present are more likely to be a consequence rather than a cause of illness. Serious doubts are raised about the validity of the application of a psychiatric label. A conviction by patients of physical illness is demonstrated to be understandable and legitimate.

(continued on page 46)

INFORMATION ON ME/CFS *(continued)*

COGNITIVE BEHAVIOURAL THERAPY IN ME/CFS

Evidence shows it is at best ineffective and at worst harmful in authentic ME/CFS.

GYNAECOLOGICAL PROBLEMS IN ME/CFS

A number of gynaecological conditions have been found to occur more frequently in women with ME/CFS, for example endometriosis is reported to occur in up to 20% of women with the disorder; cystic enlargement of the ovaries may be present and can be seen on ultrasound scan. A history of ovarian cysts, including polycystic ovaries and uterine fibroids was found in one study to be more common in patients than in controls. Prostatitis is common in men with ME/CFS.

SPECIAL PROBLEMS IN CHILDREN WITH ME/CFS

It is not widely recognised that children and adolescents can suffer from ME/CFS, which has been found in children as young as five. There may be appalling problems with ignorant authorities, with children being forcibly removed from their homes and placed in the "care" of the State and the parents accused of child abuse; one consultant paediatrician who specialises in ME/CFS is on record as confirming that the number of such cases now amounts to an epidemic. The presentation in young people may differ from that in adults. Some children require tube feeding. Education may be a particular problem. There are many horrific stories of inappropriate and damaging psychiatric interventions. The Review Article by Professor Leonard Jason et al is essential reading (Chronic Fatigue Syndrome in Children and Adolescents: A Review. Karen M Jordan, Leonard Jason et al. Journal of Adolescent and Child Health 1998;22:4-18)

SIMILARITIES AND DIFFERENCES BETWEEN ME/CFS AND FIBROMYALGIA

Although there is some overlap of symptomatology in both conditions, there are significant differences between ME/CFS and FM: the WHO lists them as separate disorders in the ICD and there are important laboratory distinctions (eg. levels of somatomedin C; substance P; CBG levels; secretion of ATP; acetylcholine sensitivity; endothelin-1 levels etc). Studies suggest that those with co-existent disorders face an additional burden of suffering and a worse outcome.

GENETIC ABNORMALITIES IN ME/CFS

There is unequivocal evidence of acquired abnormalities in numerous genes involved in energy production and with the neurological and immunological systems.

PATTERNS OF MEDICAL MISDIAGNOSIS

Misdiagnosis is very common in complex and poorly understood illness and patients are often ignored or dismissed by medical practitioners without justification. This increases their suffering. The literature abounds with evidence that patients have often been given an inappropriate label (usually by psychiatrists), and that such labels abruptly disappear when medical science and knowledge discover an underlying organic aetiology. Examples are legion, and include diabetes, hypothyroidism, pernicious anaemia, peptic ulcer, multiple sclerosis and Parkinson's disease -- in the 1940s, psychiatrists claimed that the intention tremor was due to the inner conflict of the patient who wished to masturbate but who knew it was wrong, and that the intention tremor was a manifestation of such inner conflict; it was not until the discovery of the neurotransmitters and the role of dopamine that such views were abandoned. Unfortunately, some psychiatrists seem unable learn from past experience.

(continued on page 47)

INFORMATION ON ME/CFS *(continued)*

A BRIEF SELECTION OF BIOMEDICAL REFERENCES ON ME/CFS

1957

An investigation into an unusual disease seen in epidemic and sporadic form in a general practice in Cumberland in 1955 and subsequent years. AL Wallis. Doctoral Thesis: University of Edinburgh, 1957. **(This is an excellent and accurate description that details the varying clinical picture, the abnormal physical findings and post mortem histopathology).**

1969

Disseminated Vasculomyelinopathy. Charles M Poser. Acta Neurol Scand 1969;S37:7-44. **(This details postviral infectious states and subsequent development of allergies and is highly relevant in view of recent autopsy findings of severe inflammation in the dorsal horn in the case of Sophia Mirza).**

1976

Benign Myalgic Encephalomyelitis or Epidemic Neuromyasthenia. AM Ramsay. Update: September 1976:539-542. **(This sets out the cardinal features).**

1978

An outbreak of encephalomyelitis in the Royal Free Hospital Group, London, in 1955.

Nigel Dean Compston. Postgraduate Medical Journal, November 1978:54:722-724. **(This documents the clear evidence of organic involvement of the CNS).**

1979

Clinical and biochemical findings in ten patients with Benign Myalgic Encephalomyelitis.

AM Ramsay; A Rundle. Postgraduate Medical Journal, December 1979:55:856-857. **(This describes the dominant clinical features -- abnormal muscle fatiguability and pain; circulatory impairment and hypothalamic damage; cognitive impairment – and notes impairment of cell membrane permeability).**

1981

Was it Benign Myalgic Encephalomyelitis? CS Goodwin. Lancet 1988; January 3rd: 37.

(This notes the three major features of the disease and documents abnormal physical findings).

1983

Sporadic myalgic encephalomyelitis in a rural practice. BD Keighly; EJ Bell. JRCGP June 1983:33:339-341. **(This provides a good clinical summary and notes a pattern to the complexity of symptoms).**

1985

Electrophysiological studies in the postviral fatigue syndrome. Goran A Jamal; Stig Hansen.

JNNP 1985:48:691-694. **(This documents abnormalities in muscle, including type II fibre predominance, scattered fibre necrosis; bizarre tubular structures and mitochondrial abnormalities).**

1987

Myalgic Encephalomyelitis (ME) Syndrome – an analysis of the findings in 200 patients.

J Campbell Murdoch. The New Zealand Family Physician 1987:14:51-54. **(This describes laboratory findings, including the presence of positive smooth muscle antibodies and anti-nuclear antibodies).**

1987

Phenotypic and functional deficiency of natural killer cells in patients with Chronic Fatigue Syndrome. M Caliguri, AL Komaroff et al. J Immunol 1987:139:3306-3313. **(This demonstrates abnormally low numbers of NK cells).**

1988

Chronic Fatigue Syndromes: relationship to chronic viral infections. AL Komaroff. Journal of Virological Methods 1988:21:3-10. **(This documents unusual and abnormal findings, including hepatosplenomegaly).**

1988

Allergy and the chronic fatigue syndrome. Stephen E Straus et al. J Allergy Clin Immunol 1988:81:791-795. **(This documents the laboratory evidence for an allergy that is described as “substantial”).**

(continued on page 48)

INFORMATION ON ME/CFS *(continued)*

A BRIEF SELECTION OF BIOMEDICAL REFERENCES ON ME/CFS

1991

Chronic Fatigue Syndrome: clinical condition associated with immune activation. AL Landay et al Lancet 1991;338:707-712. **(This documents evidence for three cell surface markers and notes that CD38 and HLA DR markers remain persistently raised).**

1992

A chronic illness characterised by fatigue, neurologic and immunologic disorders, and active human herpes Type 6 infection. D Buchwald, R Gallo, AL Komaroff et al. Ann Intern Med 1992;116:2:103-113.

(This describes a significantly increased CD4/CD8 ratio; brain scans show punctate subcortical areas of high signal intensity consistent with oedema or demyelination in 78% of patients, suggesting patients may have a chronic, immunologically-mediated inflammatory process of the CNS).

1993

Memory deficits associated with chronic fatigue immune dysfunction syndrome. Curt Sandman et al.

Biol Psych 1993;618-623. **(This demonstrates that cognitive impairment is seven-fold worse than in controls and depressives and is worse than assumed by CDC criteria).**

1993

Clinical presentations of chronic fatigue syndrome. AL Komaroff. Ciba Foundation Symposium 173:43-61. **(This describes ME/CFS as a "terribly destructive disease"; it describes the abnormal physical examination and compares the clinical picture with that of lupus).**

1996

Chronic Fatigue Syndrome: evaluation of a 30-criteria score and correlation with immune activation.

Hilgers A and Frank J. JCFS 1996;2:4:35-47. **(This paper notes important and consistent symptoms that are not included in the CDC 1994 case definition; these include respiratory problems,**

palpitations; chest pain; dizziness; dyspepsia; parasthesia; nausea and loss of hair. A correlation between the 30-criteria score and immunological parameters occurred in 472 of 505 patients).

1996

Autoantibodies to Nuclear Envelope Antigens in Chronic Fatigue Syndrome. K. Konstaninov et al

J Clin Invest 1996;98:8:1888-1896. **(This paper provides evidence of an autoimmune component in ME/CFS).**

1997

Elevation of Bioactive Transforming Growth Factor Beta in Serum from Patients with Chronic Fatigue Syndrome. AL Bennett, AL Komaroff et al. J Clin Immunol 1997;17:2:160-166. **(This paper documents the effects of TGF/beta on cells of the immune system and CNS and provides evidence that it may play a role in autoimmune and inflammatory disease).**

1997

Elevated apoptotic cell population in patients with Chronic Fatigue Syndrome: the pivotal role of protein kinase RNA. A Vojdani, CW Lapp et al. J Int Med 1997;242:465-478. **(This paper indicates abnormal mitotic cell division).**

1997

Chronic Fatigue Syndrome: A Disorder of Central Cholinergic Transmission. A Chaudhuri, T Dinan et al. JCFS 1997;3: (1):3 -16. **(This paper posits that the pathogenesis of ME/CFS involves up-regulation of post-synaptic cholinergic receptors).**

1998

Relationship between SPECT scans and buspirone tests in patients with ME/CFS. Richardson J; Costa DC. JCFS 1998;4:3:23-38. **(This paper provides evidence that all patients tested had hypoperfusion of the brain: 62% in the brain stem and 51% in the caudate nuclei).**

Neurally mediated hypotension and chronic fatigue syndrome. PC Rowe H Calkins. Am J Med 1998;105: (3A): 15S -21S. **(This paper documents neuroendocrine changes and shows the link with allergy).**

(continued on page 49)

INFORMATION ON ME/CFS (*continued*)

A BRIEF SELECTION OF BIOMEDICAL REFERENCES ON ME/CFS

2000

Comparative analysis of lymphocytes in lymph nodes and peripheral blood of patients with chronic fatigue syndrome. **MA Fletcher N Klimas et al.** *JCFS* 2000;7:3:65-75. *(This paper demonstrates the link with autoimmunity).*

2001

Prevalence in cerebrospinal fluid of the following infectious agents in a cohort of 12 chronic fatigue syndrome patients: HHV6 & 8; chlamydia species; mycoplasma species; EBV; CMV and Coxsackievirus. **Susan Levine.** *JCFS* 2001;9: (1-2):41-51. *(This paper provides hard evidence of a high yield of infectious agents in the cerebrospinal fluid of patients with ME/CFS).*

2002

Symptoms occurrence in persons with chronic fatigue syndrome. **LA Jason et al.** *Biological Psychology* 2002;59:1:15-27. *(This paper provides evidence of several cardiopulmonary and neurological symptoms that uniquely differentiate ME/CFS patients from controls).*

2002

Cytokine response to physical activity, with particular reference to IL-6: sources, actions and clinical implications. **Shepherd RJ.** *Crit Rev Immunol* 2002;22:3:165-182. *(This paper posits that exercise-induced modulations in cytokine expression may contribute to the allergies seen in ME/CFS).*

2003

Abnormal impedance cardiography predicts symptom severity in Chronic Fatigue Syndrome. **Peckerman A, Natelson BH et al.** *Am J Med Sci* 2003;326:2:55-60. *(This paper provides evidence of reduced cardiac output in patients with severe ME/CFS).*

2004

Altered central nervous system signal during motor performance in chronic fatigue syndrome. **Aiemionow V, Calabrese L et al.** *Clin Neurophysiol* 2004;115:10:2372-2381. *(This paper demonstrates altered CNS signals in controlling voluntary muscle).*

2005

Urinary and plasma organic acids and amino acids in chronic fatigue syndrome. **Jones MG et al.** *Clinica Chimica Acta: International Journal of Clinical Chemistry.* Epub June 28, 2005. *(This paper provides evidence for underlying inflammatory disease and for a lower threshold for muscle micro-injury).*

2005

Chronic fatigue syndrome is associated with diminished intracellular perforin. **Maher KJ,**

Klimas NG, Fletcher MA. *Clin Exp Immunol* 2005;142:3:505-511. *(This paper provides evidence of a Tcell associated cytotoxic deficit. As perforin is important in immune surveillance and the homeostasis of the immune system, its deficiency is likely to be an important factor in the pathogenesis of ME/CFS).*

ME Petition to PM Blair

Please support the E-Petition created by Konstanze Allsopp to enforce the acceptance of ME as a neurological illness.

"We the undersigned petition the Prime Minister to get the Health Service and medical profession to accept the WHO classification of ME/CFS as an organic neurological disorder and not as a psychosocial syndrome."

<http://www.investinme.org/E-Petition%202007.htm>

ME Story

My family called the doctor to the house on one occasion after I had become too weak to walk or talk and couldn't make the bathroom without assistance.

The GP advised me to go out for a jog in the sunshine.

- Cathy

International ME/CFS Conference Agenda

DAY 1 - 1st May 2007 - ME Awareness & Support Day

Start	Presenter	Presentation
08:30	<i>REGISTRATION & MEDIA INTERVIEWS</i>	
10:30	IiME	Welcome to the Conference
10:40	Norman Lamb MP	Opening Speech/Key Note Speech
	<i>RESEARCH & FUNDING – A Review of Current Work & Requirements</i>	
11:05	Dr. Derek Pheby	Case Study – Epidemiology of ME/CFS
11:30	Dr. Jonathan Kerr	Case Study - Biomedical research (A view of a biomedical research team, how it is funded, what it needs, how it could be improved, what the future research would look like)
12:00	Lunch	
	<i>MODELS for TREATMENT of ME/CFS</i>	
13:00	Professor Kenny De Meirleir	Treatments for ME/CFS Integrative & Complementary Medicine
13:30	Annette Whittemore	A Model ME/CFS Clinic - The CFS Clinic – Reno, Nevada, USA
13:55	Dr. Daniel Peterson	Experiences of Research into ME – Past, present and future
14:25	Dr. Vance Spence	Biomedical Research into ME/CFS: where does it go from here
14:45	Professor Malcolm Hooper	Future ME/CFS Projects - Research being planned & Common Aims - how to get researchers working together
15:15	Coffee/tea Break	
	<i>CURRENT ISSUES - NICE, GUIDELINES, CAMPAIGNS</i>	
15:35	Ellen Piro	NICE Guidelines – Experiences from Norway
16:00	Dr. Byron Hyde	ME and Insurance companies
16:30	Open forum	Plenary Session <ul style="list-style-type: none"> • International alliances • Guidelines • Diagnostic testing • Tissue Banks • Local Services
17:30	Adjourn	

International ME/CFS Conference Agenda

DAY 2 - 2nd May - Professionals Day

Start	Presenter	Presentation
07:45	<i>Registration & Media interviews</i>	
09:00	IiME	Welcome to the Conference
09:10	Dr. Ian Gibson MP	Key Note Speech
09:30	Professor Martin Pall	Biochemical Underpinnings of ME/CFS
10:00	Dr. Abhijit Chaudhuri	Pathology of ME/CFS
10:30	Coffee/tea Break	
10:50	Dr. Vance Spence	Vascular aspects of ME/CFS
11:20	Dr. Sarah Myhill	Treatments and Diagnosis – A GP's Perspective
11:50	Professor Kenny de Meirleir	Treatments – A ME Clinical Research Perspective Medical Research and Treatment Updates
12:30	Lunch	
13:30	Dr. Nigel Speight	Paediatrics and ME
14:00	Dr. Byron Hyde	The epidemiology, definitions and techniques of investigation of the ME and CFS patient and the resulting pathological findings or Case Studies / Thyroid Problems
14:40	Coffee/tea Break	
15:00	Dr Jonathan Kerr	Research: A Year On: Viral and Human Gene Expression, development of diagnostic test, news of clinical trials
15:30	Dr. Daniel Peterson	Biomedical Research
16:05	Professor Malcolm Hooper	Summary - Future Strategy for ME Research, Diagnosis and Treatment
16:35	All Speakers	Open forum / Questions
17:30	Adjourn	



ME Conference 2006 DVD

Still available – the IiME ME Conference 2006.

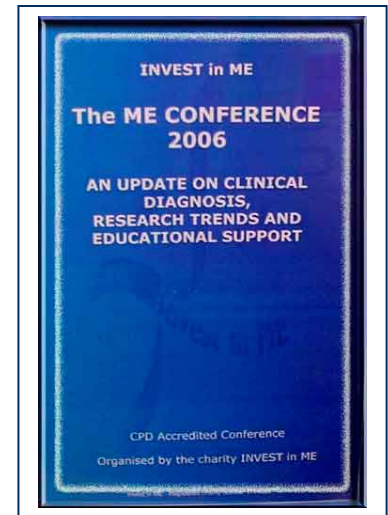
Sold in over 20 countries this is now available as an educational tool – useful for healthcare staff (GPs, paediatricians, occupational therapists and others connected with the treatment of ME), researchers, scientists, educational specialists, media, ME support groups and people with ME and their carers/parents.

Comprising 3 DVDs and a data CD the conference has the full lectures from the conference from Dr. Ian Gibson, Professor Malcolm Hooper, Dr. Byron Hyde, Dr. Jonathan Kerr, Jane Colby, Dr. Bruce Carruthers and Professor Basant Puri.

Also included are TV programmes from ITV Meridian and Norsk Puls programme about severe ME.

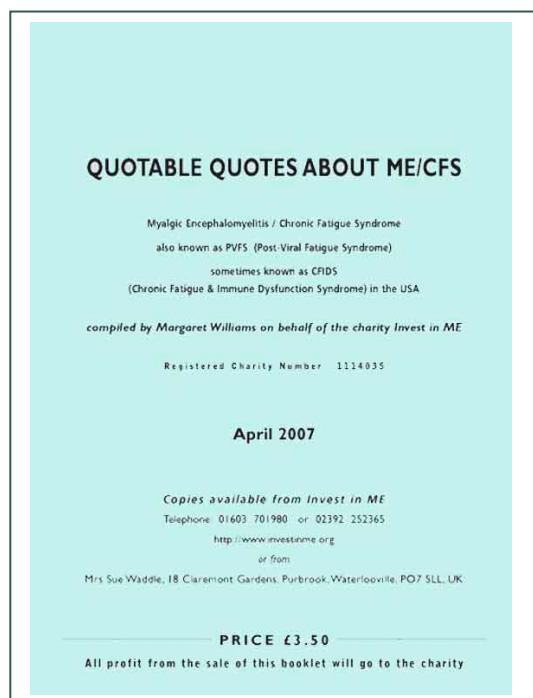
Price £13 plus p&p (£2 UK/£3 Europe and USA/Canada/Australia/New Zealand).

To order send an email to meconference2006@investinme.org entitled DVD or go to <http://www.investinme.org/tinyurl> to order online.



Order the 2007 Conference DVD

The DVD of the May 2007 conference should be available in early June. To order please email meconference@investinme.org and include your name and contact details plus the number of copies wanted and preferred mode of payment.



Quotable Quotes on ME/CFS

Available only from IiME. This 42 page booklet has been researched by Margaret Williams and contains a plethora of quotes from ME experts and from others relating to ME, ME/CFS, CFS/ME and CFS.

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