North Methven Street, Perth PH1 5PP, UK

ME RESEARCH UK

breakthrough

News of the ME research YOU are helping to fund

New Horizons

Colloquia and Conferences

The first Colloquium on ME/CFS Biomedical Research, sponsored jointly by ME Research UK and the Irish ME Trust, took place in 2006 at Glasgow Caledonian University. The event, hosted by Dr Lorna Paul, consisted of presentations by key scientists with a working interest in the illness, and was followed by a workshop on Physiotherapeutic Aspects of ME/CFS led by Dr Lorna Paul and Dr Jo Nijs from Vrije Universiteit Brussel, Belgium.

The event was targeted particularly at scientific and healthcare professionals with a working interest in ME/CFS, and the aim was to facilitate links between scientists working on the biomedical basis of ME/ CFS, and to raise awareness of the need for biomedical investigation. After a welcome and introduction by Prof. Brian Durward (Dean, School of Health and Social Care, Glasgow Caledonian University), there were scientific presentations from, among others, Prof. Jill Belch (Vascular Diseases Research Unit, University of Dundee), Dr Jonathan Kerr (Department of Cellular and Molecular Medicine, St George's University of London) and Dr Julia Newton (School of Clinical Medical Sciences, University of Newcastle).

Building on the success of this event, we have organised a larger "New Horizons International Conference on ME/CFS Biomedical Research" for Friday 25th May 2007 at the Edinburgh Conference Centre, Heriot-Watt University, Edinburgh. We hope to make this an annual event, the location of which will vary from year to year. ●

SPRING 2007

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WHAT IS ME/CFS?

Myalgic encephalomyelitis/ encephalopathy (ME) is characterised by a range of neurological symptoms and signs, muscle pain with intense physical or mental exhaustion, relapses, and specific cognitive disabilities.

During the 1990s, the term 'chronic fatigue syndrome' (CFS) came into vogue. Since there was no specific diagnostic test for ME, and since post-exercise 'fatigue' was one of its prominent symptoms, people with ME began to be diagnosed with 'CFS'. At present, efforts are being made to revise the definitions of both ME and CFS, and meanwhile the term ME/ CFS is used.

ME/CFS affects 120,000 to 240,000 people in the UK, and it is classified by the World Health Organisation as a neurological illness (ICD10: G93.3). Most people with ME/CFS are unable to work to full capacity, and 25% are severely disabled, some house or bed-bound. Little support is available to their families and carers. The cause of the illness is unknown, and no cure or universally effective treatment has yet been found.

A report to the Chief Medical Officer of England in 2002 states "ME/CFS is a genuine illness and imposes a substantial burden on the health of the UK population. Improvement of health and social care for people affected by the condition is an urgent challenge."

Uncovering the Truth

Research Findings from the University of Dundee

Dr Neil Abbot, Director of Operations, ME Research UK, and Honorary Fellow, 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 is certainly clear from the output of Prof. Belch and Drs Kennedy, Khan and Newton at the Vascular Diseases Research Unit at the University of Dundee which, with funding from ME Research UK, has uncovered a range of potentially important findings in people with ME/CFS, reported in scientific papers from 2003 to 2006. These include:

Increased oxidative stress
The researchers found a pattern of significantly increased oxidative stress: increased oxLDL and isoprostanes with decreased HDL and GSH (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.

Abnormal acetylcholine metabolism
Acetylcholine is a substance produced by the layer of endothelial cells lining all blood vessels, causing them to open. The group found that vascular responses to acetylcholine are increased compared with matched control subjects (Spence et al, 2000; Khan et al, 2004). 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.

Increased neutrophil apoptosis
Data from 2005 indicate that ME/CFS patients have detectable abnormalities in a type of white blood cell (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 and 2004). Accompanying these markers of neutrophil apoptosis, they have found that high-sensitivity C-reactive protein levels, recognised as a marker of the inflammatory process, were also significantly increased.

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, 2004). 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.).

All these results are very exciting, though it is important to recognize that these tests are not yet diagnostic markers. They show that if scientific effort and funding are directed towards a problem, researchers 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. ●

New Horizons

International Conference on ME/CFS Research

Hosted and organised by ME Research UK, and co-sponsored by the Irish ME Trust, the New Horizons International Conference on ME/CFS Biomedical Research will take place on Friday 25th May 2007 at the Edinburgh Conference Centre, Heriot-Watt University, Edinburgh. Building on the success of our Colloquium last year, we hope this international conference will become an annual event changing location from year to year.

As ME/CFS biomedical research is very varied, spanning many scientific disciplines and involving a wide range of healthcare professionals, this research conference will provide the opportunity for researchers and healthcare professionals within ME/CFS to present their latest work, share ideas and identify key challenges for the future. The full day's programme, which we are finalising at present, will consist of invited keynote lectures and shorter research presentations, and will be of interest to a wide range of professionals, people with ME and observers alike.

The conference facilities within the James Watt Centre are purpose built and disability-friendly, in an attractive campus setting, near the airport and just outside the city centre, with free on-site parking. In addition, bed and breakfast accommodation (approx. £40 per night) is available on-campus near the venue.

Registration will be from 8.30 am, and the expected finish is 5 pm. Included in the £60 registration fee are a delegate pack with detailed lecture notes, finger-buffet lunch, and morning and afternoon coffee/tea breaks, served on-site.

This conference will be a key element of ME Awareness Month 2007 — an important time for people with ME globally, which is the reason Invest in ME and ME Research UK will be working together to "energise ME awareness" over the whole of May 2007, opening and closing it with an event to remember. The awareness-raising 2nd International IiME ME Conference at Westminster, London on 1st to 2nd May will **open** the month, and the International Conference on ME/CFS Biomedical Research at Heriot-Watt University in Edinburgh will **close** the month.

If you would like to attend the Edinburgh conference, please contact our headquarters for further details. We can send you a booking form and conference flyer with registration form (which you can also download from our website at www.meresearch.org.uk). ●

The team at ME Research UK send our best wishes to all our supporters for the year ahead. We have decided not to send Christmas cards to individual supporters from now on, to keep costs down. Rest assured your support is vital and allows us to continue energising ME research.

WHAT IS ME Research UK?

ME Research UK is a medical research charity which commissions and funds scientific (biomedical) investigation into the causes and treatment of ME/CFS. We also have a mission to "Energise ME Research", and our in-house team identifies potentially important biomedical research projects, publishes scientific papers, produces high-quality professional reviews and reports, and organises meetings and conferences.

Recognising that much of the existing research into ME has concentrated on psychological interventions designed to "manage" the illness, ME Research UK believes that biomedical research is urgently required and is what most patients and carers want to see. For this, researchers with fresh, novel ideas have to be recruited and encouraged to undertake research in this field. This is the most difficult task of all, and ME Research UK sees its role at this leading edge: to give help to biomedical scientists for novel research projects that would otherwise not be funded, and to support research groups to the stage where they can apply to major funding agencies for further support based on their initial data.

With your help — and building on our close working relationships with other ME/CFS organisations around the world — ME Research UK can be a force for change, and a source of real hope for the thousands of people with this debilitating illness.

ON THE WEB

www.meresearch.org.uk

ME Research UK's website is a source of news, education and information on ME/CFS research and other issues of interest to biomedical researchers, healthcare professionals, people with the illness and their carers, and the general public.

The **RESEARCH** pages contain summaries and explanations of projects funded by us, reviews of the scientific literature, recently-published ME Research UK articles, and details of our funding procedures.

In the **INFORMATION** section, you can find a collection of literature on ME/CFS and its consequences, a database of abstracts of all ME/CFS research papers from 1956 to 2006, and ME Research UK's own documents discussing and analysing important issues.

The **SUPPORT** section contains information and advice on accessing social care support for people with ME/CFS.

The website also keeps you up-to-date with the latest ME/CFS research news, and with Friends of ME Research UK activities.

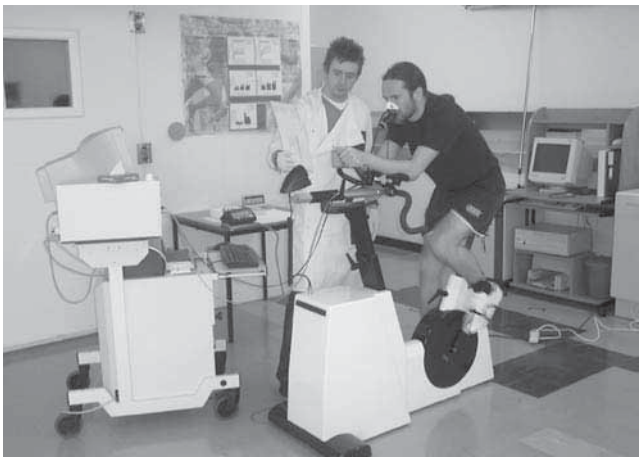
Interleukin-6 and its Receptors

There have been some suggestions that the "fatigue" in ME/CFS could be associated with limitations in the use or supply of fuel by the tissues. If so, an understanding of interleukin-6 (IL-6) and its associated receptors could be important, since IL-6 is produced by working skeletal muscle and is also a key component of the body's response to the illness. In support of a role for IL-6 is the observation that oxidative stress is elevated and prolonged in ME/CFS patients (Jammes et al, 2005) and related to ME/CFS symptoms (Kennedy et al, 2005), since oxidative stress is a known promoter of IL-6 production.

Some studies have indicated that ME/CFS patients do not have raised levels of IL-6 and other cytokines in the blood at rest, but IL-6 requires receptors to be biologically active. Although these are present in some tissue membranes, skeletal muscle, fat tissue and endothelial cells have few or none. Therefore, a crucial point is to investigate not only IL-6 but also its receptors. As it is exercise that brings on symptoms in most people with ME/CFS, at least in the early stages of the illness, perhaps researchers ought to be looking at changes during exercise rather than at rest. This aspect particularly interests Professor Myra Nimmo, of the Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, who is a metabolic physiologist internationally renowned for work in exercise physiology. She says, "Exercise offers the opportunity to examine patients in an exacerbated state, yet many studies to date have not clearly categorised the exercise regimen and, since incremental maximal tests are essentially limited by cardiorespiratory fitness, metabolic limitations may be more clearly identified through the use of a sub-maximal protocol."

Professor Nimmo and Mark Robinson (who is pictured below) have been conducting an ME Research UK-funded pilot study of 6 men with ME/CFS and 6 healthy control subjects matched for age, physical activity and body mass. Each person undertook an exercise bout at 90% lactate threshold, allowing a "matching" of the metabolic load between controls and patients. All subjects were required to visit the laboratory twice, the first being for identification of the lactate threshold. On the second occasion, subjects were exercised at their identified exercise load in the morning before eating. Subjects were then given standardised meals for the following 24 hours (not very palatable, unfortunately), and blood samples were taken pre and post-exercise and at intervals throughout the 24 hours.

The results are at the analysis stage at present, and Prof. Nimmo comments, "An understanding of the IL-6 response to exercise could more clearly define any metabolic perturbance in these patients, and contribute to the development of a therapeutic drug intervention. For example, blockade of sIL-6R by its natural antagonist has been shown to inhibit arthritis progression, a disease expressing not dissimilar symptoms to ME/CFS." ●



Leaving Patients in a NICE Pickle

Late in 2006, the National Institute for Clinical Excellence (NICE) published its "ME/CFS Guideline Draft For Consultation", and raised a storm of protest from Registered Stakeholders, including ME Research UK. Its decisions often raise a rumpus, but there is something unusual — unique, in fact — about the current uproar. Today, almost certainly for the first time since it started work in April 1999, NICE is faced with a united body of patient-based opinion which does NOT want the guideline it has produced, certainly not in its current form, and if push comes to shove would rather have no guideline on ME/CFS than the one on offer.

In short, the draft is unfit for purpose — i.e., for informing the diagnosis and management of ME/CFS patients — primarily because it flags up as treatments for the illness psychosocial management and coping strategies that at best have an adjunctive role to play. Patient-based charities and self-help groups (and there are around 20,000 members of these in the UK alone) recognise this, and can foresee that the major recommendations of the guideline will not, unfortunately, solve the problem on the ground.

This is because the Institute has not got to grips with core issues surrounding ME/CFS. The first, and most central, is the problem of diagnosis: whichever definition is used, ME/CFS is widely recognised to be an impossibly wide diagnostic marquis and to contain different patient groups; the formation of clinical guidance inevitably raises the question of guidance for what and for whom. The second problem concerns the randomised controlled trial evidence upon which NICE puts a premium, and the devaluation of evidence from scientific studies and surveys. In this illness, the evidence-base is skewed towards a small group of mildly positive trials on psychosocial strategies; thus, instead of finding the "best" evidence garnered from the work of a range of biomedical and biopsychosocial scientists working on a level playing field, what is found is quite modest evidence in a forgotten field put there by proponents of psychosocial strategies such as cognitive behavioural therapy (CBT). Multiple sclerosis with the formal evidence-base that currently exists for ME/CFS would be no less a physical illness, and the non-specific management and coping strategies would be no more specifically effective for the underlying disease, yet these adjunctive strategies have an unduly prominent role in the Institute's draft guideline. The Table on the right illustrates this nicely. It shows that CBT is recommended as a specific treatment for psychological illnesses, but not for physical conditions. Except that is for ME/CFS.

The unfitness of this guideline draft is a terrible blow to people with ME/CFS, and we think that it should be withdrawn pending a complete overhaul.

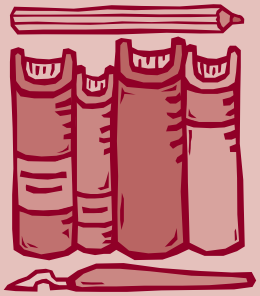
ME Research UK's full 9000-word critique of the draft NICE guideline can be read at our website. ●

TABLE

NICE Clinical Guidance recommendations on the use of CBT for 19 different clinical conditions

Is CBT postulated to be a specific treatment for the condition (Clinical Guideline number)?	
Anxiety (22)	**YES**
Bipolar disorder (38)	**YES**
Depression (23)	**YES**
Eating disorders (9)	**YES**
Obsessive-compulsive disorder (31)	**YES**
Schizophrenia (1)	**YES**
Chronic pulmonary disease (12)	**NO**
Dementia (42)	**NO**
Dyspepsia (17)	**NO**
Type 1 diabetes (15)	**NO**
Hypertension (34)	**NO**
Lung cancer (24)	**NO**
Multiple sclerosis (8)	**NO**
The epilepsies (20)	**NO**
Parkinson's disease (35)	**NO**
Familial breast cancer (41)	**NO**
Tuberculosis (33)	**NO**
Chronic heart failure (5)	**NO**
ME/CFS Draft Guideline 2006	**YES**

MERUK ARTICLES



ME Research UK produces reviews of scientific research into ME/CFS, and publishes general articles on the topic to raise awareness of the issues. Recent examples include:

A Scientific 'Signature' for ME/CFS?
An essay on current developments in genetic research in ME/CFS.

The Muscle in ME: It Isn't All Deconditioning!
A "research update" overview, originally published in the magazine Interaction, in 2005.

New Developments in the Biology of ME/CFS
Our report on the Royal Society of Edinburgh Workshop in 2004.

Severely Overlooked by Science
An overview with the 25% ME Group (with which we have close links) of research on the most severely affected ME/CFS patients.

Advances in the Biomedical Investigation of ME/CFS
Describing some recent developments in biomedical research, as well as some of the problems.

Parliamentary Inquiry

Gibson report calls for a research summit

The Group on Scientific Research into ME, headed by Dr Ian Gibson (MP for Norwich North), which spent almost a year investigating ME/CFS, finally delivered its report at the end of 2006. As the report makes clear, *"The principle actuality remains, that there exists a serious disease, which causes much suffering for patients... This is the baseline from which all else should follow."* It goes on to address a range of issues from research to putative treatments and benefit entitlements.

Overall, the conclusions are a step forward for people with ME/CFS. While recognising that opinion is split on definitions, the Group found the 2003 Canadian Clinical Working Case Definition of the illness — which allows for subgroups based on symptom clusters — to be *"a useful contribution to the attempt to define the clinical condition"*. Again, the Group was very interested in the international evidence submitted, and in a key section, it emphasises, *"Various clinical and epidemiological research studies in countries around the world have suggested ME/CFS to have a biomedical cause... The Group believes the UK should take this opportunity to lead the way in encouraging biomedical research into potential causes."* Specifically, the Group calls for a further "Inquiry into the Scientific Evidence for ME/CFS", commissioned by government and *"undertaken by an independent panel of scientific and medical experts, including virologists, immunologists, biochemists, etc. who can objectively assess the relevance and importance of the international scientific data"*.

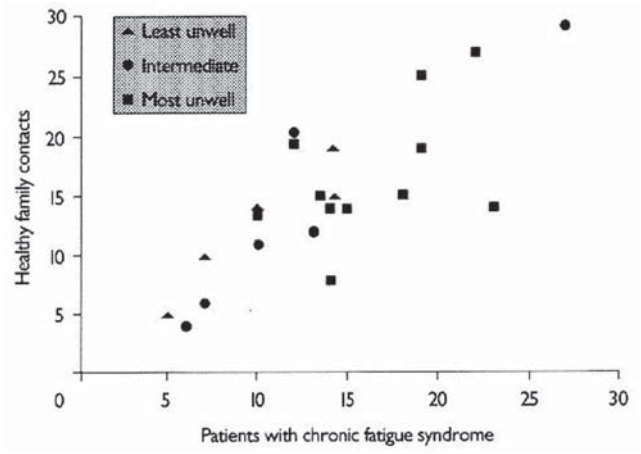
Among the specific points, the report calls for treatment to be given as early as possible, when symptoms first begin. It also questions why the Department of Health does not keep or collect data pertaining to the number of people in the UK with the illness. And it points out that no representative who appeared at the five oral hearings proposed that ME/CFS was entirely psychosocial, begging the question why psychosocial aspects have taken such a prominent role in the UK. Crucially, it calls on the Medical Research Council (MRC) to encourage wide ranging research, on a similar basis to the AIDS programme funded previously by the council. And as regards the immediate future the report is clear: the MRC should, *"...in order to overcome the perception of bias in their decisions… assign at least an equivalent amount of funding (£11 million) to biomedical research as they have done to psychosocial research... It is an illness whose time has certainly come."*

We can only echo Dr Gibson's own comments as the report was published: *"At last there is an inquiry which identifies the seriousness of ME/CFS. For too long the patient's voice has been left out of the debate."* ●

The photograph left shows (L to R) Dr Neil Abbot (our Director of Operations), The Countess of Mar, Dr Vance Spence (our Chairman), Doris Jones (Environmental Issues Forum) and Dr Jonathan Kerr (St George's University of London) outside the House of Lords after our presentation at the third oral hearing of the Inquiry.

Activated But Ignored

Time marches on, but sometimes it can seem to stand still, at least where research into ME/CFS is concerned. One of the earliest biomedical investigations into ME/CFS occurred at the University of Dundee in 1993, spurred by an observation of Prof. Jay Levy that people with ME/CFS have raised levels of



an "activation marker" on white blood cells. This marker is CD38 (cluster of differentiation 38), a glycoprotein and marker of cell activation found on the surface of many immune cells. Interestingly, it has subsequently been linked with HIV infection, type 2 diabetes and bone metabolism, as well as some genetically determined conditions. It has also been used as a prognostic marker in leukaemia. The point about Prof. Levy's observations was that they indicated that immune activation may be associated with ME/CFS.

The team at Dundee investigated the association between immune activation and delayed hypersensitivity responses (using Multitest antigens and tuberculin skin tests) in 68 people with ME/CFS, 22 family contacts and 15 unrelated healthy people. They assessed and evaluated peripheral blood activation markers (CD8, CD38/CD11b/HLA-DR) using flow cytometry. Patients were classified into three groups on the basis of current severity of illness and mobility.

An intriguing finding was that the most unwell group of ME/CFS patients had higher levels of CD8, CD38 T-cells than those who were less ill (BMJ, 14 May 1994). But the most unexpected finding was a positive relationship ($r=0.78$, $p<0.00002$) between CD38 activation markers in patients and their close family contacts (see graph). These pairs were not blood relatives, and it could be that the relationship was caused by some environmental factor. However, because CD38 is a marker of immune activation, and is raised in infections, it could be that an infectious agent affects both patients and household contacts, but causes symptoms only in patients. As Bob Potts, Head Biomedical Scientist in Immunology (pictured below) who analysed the original data says, *"Like many intriguing biomedical observations on ME/CFS patients, this finding has never been followed up, or reproduction attempted by any other research group in the world."*

Yet, it is only one of the many observations on ME/CFS patients which lie ignored in the scientific literature, and which could form the basis of a future breakthrough if pursued. ●

CURRENT RESEARCH PROJECTS

Our primary aim is to fund high-quality projects to investigate the causes, mechanisms and symptoms of ME/CFS, and ultimately to develop effective treatments. At present, we fund the work of a growing number of scientists. Some of these are listed below, while others are going through our in-house assessment procedure.

Post-exertional malaise in ME/CFS: the role of intracellular immunity and sensory processing
Dr Jo Nijs, University College Antwerp

Inflammation and arterial stiffness in patients with ME/CFS
Dr Faisel Khan, University of Dundee

Non-invasive structural and functional neuroimaging in ME/CFS
Dr Kishore Bhakoo and Prof. Basant Puri, Imperial College London

Prevalence of autonomic dysfunction and relationship with outcome in ME/CFS
Dr Julia Newton, University of Newcastle

An investigation into biochemical and blood flow aspects of ME/CFS in children
Dr Gwen Kennedy, University of Dundee

The response of interleukin-6 and its receptors to a standardised exercise challenge
Professor Myra Nimmo, University of Strathclyde

Effects of muscle fatigue on H-reflex excitability in subjects with ME/CFS
Dr Les Wood, Glasgow Caledonian University

SETTING THE AGENDA

ME Research UK's publications and presentations offering analysis and discussion of public policy issues.

Smoke and Mirrors
Our 9000-word submission to NICE regarding its 2006 Draft Guideline on ME/CFS.

Research into ME/CFS in the UK: Can the NRR inform future policy?
Our analysis of ME/CFS research funding sources.

Who Cares?
Our submission on care pathways to the Scottish Executive's Short-Life Action Group on CFS/ME.

Shattered — Life with ME
by Lynn Michell, who collaborated closely with us during the writing of this book. Contains a Foreword and Appendix by ME Research UK.

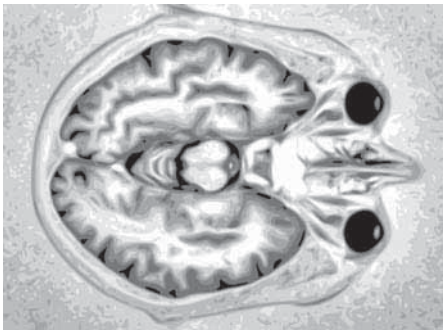
Cross Party Parliamentary Group on ME
Presentation given in 2005 to the Scottish Parliament by our Chairman Dr Spence.

Database of Research Publications
Contains more than 3,000 research abstracts on ME/CFS, from 1956 to the present.

Most of these and other documents can be found on our website. See the sidebar on page 4.

Recent Research from

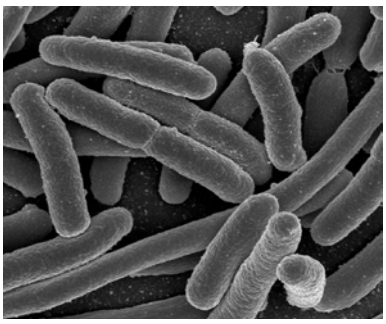
Abnormal patterns of brain activation



Cognitive problems, such as with memory and concentration, are reported by many people with ME/CFS — indeed, their presence forms part of the 2003 Canadian Clinical Working Case Definition of the illness. Dr Xavier Caseras of the Universitat Autonoma de Barcelona, Spain (Psychosom Med, 2006) used functional magnetic resonance imaging to examine the neural basis in the brain for deficits in working memory in 17 ME/CFS patients and 12 healthy control subjects. All were scanned while performing a parametric version of the n-back task (during which people see a series of capital letters on a projection screen and have to press a button whenever they recognise that a letter has been presented before).

ME/CFS patients showed reduced increases in activation in parietal and dorsolateral prefrontal regions, and also reduced decreases in activation in ventromedial prefrontal regions, consistent with the notion that the working memory system is compromised. While the causes of these abnormal patterns of brain activation remain elusive, the neural data do confirm what patients report, and partly replicate previous findings of working memory neural abnormalities. ●

Enterobacteria leaking



Some researchers think that ME/CFS might not only be triggered by viral and bacterial infections or physical stresses, but also by an increased permeability of the gut barrier, which might allow through endotoxins (part of the outer cell wall of bacteria) secreted by Gram-negative enterobacteria, leading to an immune response by the body. The Maes group in Belgium (J Affect Disord, 2006) decided to investigate this indirectly from blood levels of IgA and IgM to lipopolysaccharides of bacteria, such as *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. They found that the prevalence of abnormally increased IgA levels was significantly higher in the 15 ME/CFS patients (66.7%) than in the 11 normal controls (0%) and in 14 partial ME/CFS patients (7.1%).

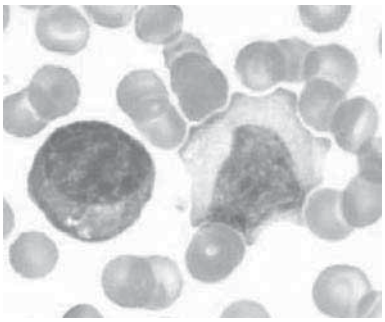
In addition, serum IgA levels were significantly correlated to the severity of illness ($p=0.002$), and with symptoms like irritable bowel ($p=0.0001$). Could it be that gut-intestinal permeability and enterobacteria are involved in the development or maintenance of the illness? The authors recommend that patients with ME/CFS should be checked with the standard ELISA IgA panel and, if positive, treated for increased gut permeability. ●

Around the World

Does D-ribose improve symptoms?

Treatment-related studies in ME/CFS are badly needed, as people with the illness often point out. So it was interesting to see an uncontrolled pilot study from the Fibromyalgia and Fatigue Centers, Dallas, Texas (Journal of Alternative and Complementary Medicine, 2006) which looked at the effect of D-Ribose three times daily, to a maximum dose of 280 g, in 41 people diagnosed with ME/CFS or fibromyalgia. The hypothesis was that since both conditions are often associated with impaired cellular energy metabolism, D-ribose — which apparently increases cellular energy synthesis in heart and skeletal muscle — might improve symptoms. Patients reported a significant improvement during the study in all five visual analogue scale categories: energy, sleep, mental clarity, pain intensity and well-being, as well as an improvement in their global assessment of their condition (62.9% saying that they subjectively felt somewhat or much better). Of course, these results need confirming in a blinded trial with a placebo arm, since there is a well-recognised tendency for small uncontrolled studies to have positive results that are not later confirmed. Nevertheless, it is heartening to see studies of dietary supplements, since this is an area where there are many claims but little evidence. ●

The infection which never goes away



The British Medical Journal has published an important report (Hickie et al, BMJ, 16 Sep 2006) of a prospective cohort study following 253 patients from the time of acute infection with Epstein-Barr virus (glandular fever), *Coxiella burnetii* (Q fever) or Ross River virus (epidemic polyarthritis) to the possible development of ME/CFS-like illness. Prolonged illness characterised by disabling fatigue, musculoskeletal pain, neurocognitive difficulties and mood disturbance developed in 28 (11%) of the group, who then met the diagnostic criteria for ME/CFS after 6 months or more. Importantly, ME/CFS was predicted largely by the severity of the acute illness rather than by demographic or psychological factors. The authors' main point was that after clinical infection with several different viral and non-viral micro-organisms, a post-infective "fatigue syndrome" can indeed occur, supporting the many reports in the scientific literature (from 1934 onwards) of the sometimes-epidemic post-infectious illness of a thousand names which we now call ME. ●

The forward march of CBT halted?

Cognitive behavioural therapy (CBT) is a form of psychotherapy used primarily for psychiatric illnesses. There have been many studies on the apparent usefulness of CBT as a treatment in ME/CFS. The most recent of these (O'Dowd et al, Health Technology Assessment 2006) has reported that patients receiving group CBT did not significantly improve cognitive function, quality of life, employment status or healthcare utility. While some other improvements were reported, there was no evidence that the treatment restored normal levels of function for most patients. While the reasons for this are unclear, it does not bode well for attempts to roll out therapist-intensive, expensive CBT facilities for the physical illness ME/CFS.

Heading towards a treatment?

A paper by Dr Jonathan Kerr in the Journal of Clinical Pathology (2006) describes current research priorities in ME/CFS, and the possibility of a diagnostic test and treatments. Gene expression has been studied in people with the illness, and the most predominant functional theme is that of immunity and defence. However, the precise gene signature and metabolic pathways involved are not yet known, although this is currently being addressed. It is important to ensure that any gene signature is specific to ME/CFS and does not occur in other diseases. Dr Kerr's group is developing a "diagnostic test" using SELDI-TOF mass spectrometry following a pilot study in which putative biomarkers were identified. The group believes interferon-beta and one of the anti-tumour necrosis factor-alpha drugs are potential novel treatments.

FRIENDS SCHEME

Our Friends scheme provides the core support needed for our work to continue. There are three categories: **Individual Friends**, **Corporate Friends** and **Group Friends**, all sharing our medium to long-term aim of a biomedical breakthrough in ME/CFS, and representing many thousands of patients and carers across the globe.

Individual Friends can give their support in a variety of ways, such as fundraising, regular donation by standing order, taking a collection box, or by just spreading the word: one of the most efficient ways of getting our work known.

The **Group Friends** scheme is for local ME support groups, and there are currently 25 groups informally signed-up. The Groups range from Castleford to Solihull & Birmingham, and from Aberdeen to Warwickshire. The full list can be found on the Friends of MERUK section of our website.

Corporate Friends is designed for larger independent organisations — corporations, larger registered charities, companies, businesses — that share our aims, and the scheme brings collective power to the drive to "energise ME research".

With the help of all our Friends, we can continue to be a force for change, and a source of real hope for the thousands of people with this debilitating illness.

High Peak Trail

The High Peak Railway is one of the most extraordinary feats of 19th century railway engineering. Yet the thousands of excited spectators who cheered its opening in June 1830 never imagined that exactly 176 years later six intrepid adventurers would be walking the High Peak Trail for ME Research UK.

The lads all work at Nissan Motor Parts Centre in Lutterworth, and were encouraged in their quest by Jane Shaw, who has had ME for a number of years and is one of our Friends and a member of the Warwickshire Network for ME. The guys covered the 17.5 miles of traffic-free trail which supports abundant wildlife and where many wildflowers flourish, including cowslips, wild strawberry and thyme.

Works Manager Bruce Taylor presented a cheque for £1,143 to Jane Shaw, who received it on our behalf. Thank you Nissan, Jane and family, and the guys for helping us climb the biomedical research mountain by yomping the High Peaks of Derbyshire! ●

Old Time Music Hall

Ladies and gentlemen. Phenomenal felicitations and splendidly stupendous salutations are due to the Victory Players of Balcombe who donated the profits from their Old Time Music Hall evenings to ME Research UK.

Enthusiasm, entertainment and enjoyment were the hallmarks of the bubbling Old Time Music Hall, and leading this rowdy extravaganza was the ebullient Chairman Rodney Saunders, full of excruciating introductions and innuendos, oozing bonhomie and egging the audience on to even greater excesses.

There was the inevitable over-acted Victorian melodrama featuring a wicked landlord (boos), drunken guardian (oohs), fair maiden (aahs) and rescuing hero (cheers). The photo shows Rodney and Barbara Saunders presenting the cheque for £1,582.69 to Dr Vance Spence at The Gateway. ●

Belfast Fundraising Blitz

Paul and Antoinette Christie had the marvellous idea to hold a series of fundraisers to raise awareness of the illness that has severely affected their son David. Only three years ago, at the age of ten, he lifted the national title for Jujitsu, but these days David faces enormous difficulty getting out of bed. Now in constant pain and always exhausted, he has not returned to school and has since been diagnosed with ME.

Antoinette was determined to raise awareness of the condition by holding a series of events. The first was a disco at Davitt's GAC with a raffle of goods donated by local businesses. Then Antoinette's friends and family sold blue ribbons in local chemists, and approached local shops directly for donations. Finally, a bash in the Devenish Arms Complex included Elvis impersonator Jim Brown and an auction including Steve Collins-signed boxing gloves.

The series of events raised over £3,000 for ME research. The photo shows Antoinette, Paul and David's elder brother Paul. ●

Mount Kilimanjaro Climb

In September 2006, Simon Winnall and Ian Winstanley embarked on a great expedition to North-East Tanzania to climb Mount Kilimanjaro, the highest peak in Africa at 5,895 m. Simon and Ian funded the trip themselves, so all the money raised went towards our ME research programme.

In December, Simon and Ian presented the cheque to Dr Richard Taylor, MP for Wyre Forest and Vice Chair of the Parliamentary Inquiry on Scientific Research into ME, who accepted it on our behalf at the Worcestershire ME Support Group.

Simon's sister, Nikki, has suffered from severe ME for the last eight years and is currently bed-bound with bouts of total paralysis, hence their wish to use the expedition to raise funds for research. As our Chairman, Dr Vance Spence, says, "I was a mountain climber myself before I got ill, so I am full of admiration and send our thanks." ●

A MESSAGE FROM OUR PATRONS

"ME is a substantial medical and social problem, yet relatively little research has been conducted into its causes and consequences.

The Countess of Mar

"A recent report to the Chief Medical Officer said that a programme of research on all aspects of the illness is urgently needed, and that improvement of health and social care is an urgent challenge.

Roger Jefcoate, CBE

"Given the recent sea change in the public perception of ME, and the possibility that ME patients will now be encouraged and supported rather than derided and scorned, we hope that ME Research UK's scientific and policy research will lead the way towards a treatment and cure for people with ME. Please help us to make a real difference to the lives of people with ME."

To allow us to press ahead with our mission to Energise ME Research, please consider responding to our Standing Order appeal.

ME Research UK receives no public money and relies entirely on donations from ordinary people. It is vitally important that all our supporters understand that we are one of the very few charities in the world funding biomedical research into ME/CFS, and raising awareness of the issues in a truly professional manner.

Help us to make the breakthrough that patients need and deserve by completing the standing order form on this page, or by donating through the online giving facility via our website.

Please send this form to:

ME Research UK
The Gateway
North Methven Street
Perth PH1 5PP, UK

Tel: 01738 451234
Email: meruk@pkavs.org.uk
www.meresearch.org.uk

For office use only:

Clydesdale Bank
23 South Methven Street, Perth (82-67-09) for the credit of ME Research UK, a/c no. 50419466

Bank reference number:

_____

Standing Order Form

1 **Name** _____

Address _____

_____

Postcode _____

Telephone _____

E-mail address _____

2 **To the Manager**

Bank/Building Society _____

Branch address _____

_____

Postcode _____

3 **Name of account holder(s)** _____

Account number _____

Branch sort code _____

4 **Please arrange to debit my/our account with the sum of £** _____

On the _____ **day of each month until further notice**

Starting on _____

5 **Pay to: Clydesdale Bank, 23 South Methven Street, Perth PH1 5PQ, UK**
Account: ME Research UK, Account no: 50419466, Branch code: 82-67-09

6 If you are a UK taxpayer, under the Government's Gift Aid scheme ME Research UK can reclaim the tax you have already paid on your gift. This means that your donation can increase by nearly a third at no extra cost to you. It doesn't matter what tax rate you pay as long as you pay an amount of income or capital gains tax equal to the tax we reclaim on your donations in that financial year. Please inform us of changes in your tax status. Please indicate below if you would like ME Research UK to reclaim the tax on your gift.

○ **Please treat this and any future donations I make to ME Research UK, and all payments I have made since 6th April 2000, as Gift Aid donations.**

7 **Signature** _____ **Date** _____

Thank you for your support