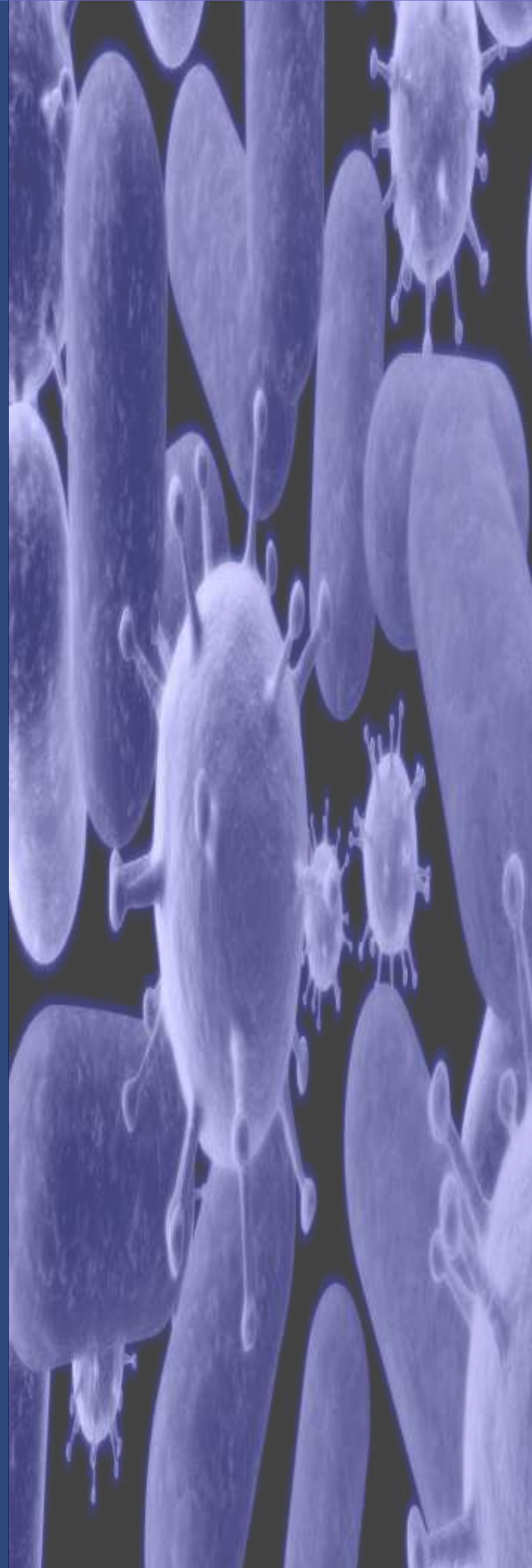


**The
Journal
of
iIME**

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LOST VOICES

The name '**Lost Voices**' refers both to the fact that people who are severely ill with ME are generally not in a position to make themselves heard, and also to the way that the prejudiced denial of ME - as an 'aberrant belief' rather than a devastating physical illness - has meant that often others are incapable of actually hearing and seeing what is being said and shown.

'**Lost Voices**' is primarily written by people affected by severe ME and clearly and movingly shows the evidence of the devastating impact this physical disease has on individuals and their

carers and families. It illustrates the plight of ME sufferers and can help change a widespread lack of comprehension about the disease based on general misinformation, vague definitions and manufactured statistics,

The book also contains facts about ME with contributions from experts such as Dr. John Chia, Professor Leonard Jason and Annette Whittemore.

Please buy this book - for yourself or for friends, relatives or for your GP - or suggest it as a gift for others to buy.



To order '**Lost Voices**'

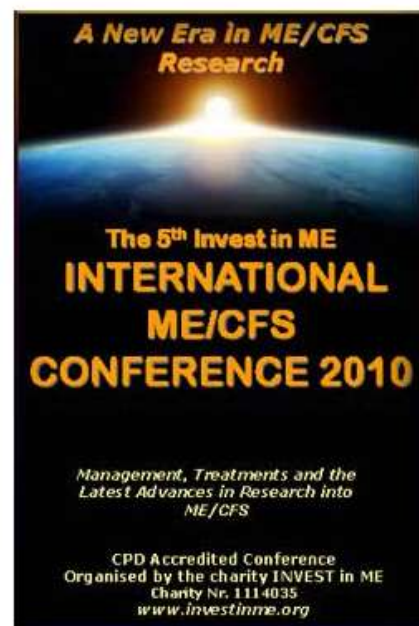
Email to
info@investinme.org

or go to our web page at
http://www.investinme.org/LostVoicesBook/liME_LostVoices_home.htm

liME Conference DVDs

These Invest in ME conference DVDs are professionally filmed and authored DVD sets consisting of four discs in Dolby stereo and in PAL (European) or NTSC (USA/Canada) format. They contain all of the presentations from Invest in ME International ME/CFS Conferences (2006 – 2011). Also included in the DVD sets are interviews with ME presenters, news stories and round-table discussions. These Invest in ME conference DVDs have been sold in over 20 countries and are available as an educational tool – useful for healthcare staff, researchers, scientists, educational specialists, media, ME support groups and people with ME and their carers/parents. Full details can be found at -
<http://www.investinme.org/InfoCentre%20Education%20Homepage.htm>

or via emailing Invest in ME at info@investinme.org





Inside This Issue

- 3 Editorial
- 10 Using
Cardiopulmonary
Exercise Testing to
Evaluate Fatigue and
Post-Exertional
Malaise in ME/CFS
- 13 The Media and ME
- 18 Letter from America
- 22 International Science
Symposium on ME
- 30 A UK Centre for
Biomedical Research
into ME
- 34 *The Involvement of the
PACE Trial Principal
Investigators and the
Director of the Clinical
Trials Unit with the DWP*
- 42 PACE is dead, long
live PACE?
- 55 CFS Education in USA
- 47 Presenters at liME
Conference
- 55 Conference Agenda

Invest in ME

(UK Charity Nr. 1114035)

PO BOX 561

Eastleigh SO50 0GQ

Hampshire, UK

Tel: 02380 251719

07759 349743

E-mail: info@investinme.org

Web: www.investinme.org

This is our seventh Journal of liME and forms part of each delegate's conference pack at the 6th Invest in ME International ME/CFS Conference 2011. The Journal of liME was created as a means of providing a broad spectrum of information on ME/CFS, combining biomedical research, information, news, views, stories and other articles relating to myalgic encephalomyelitis (ME/CFS). Our aim has always been to distribute this for free four times a year. However, due to the current size and financial limitations of liME we can only provide a snapshot of the wealth of experience which already exists and continues to increase and currently we are only able to publish a maximum of two copies a year. We hope to change that in the future.

Some years ago we wondered if a sea change was occurring in the perception of ME based on good science, objective data, effective advocacy and a long-overdue realisation from government and healthcare organisations (albeit forced by pressure from patient groups and researchers) that obfuscation and systemic bias in the healthcare services are no just or effective way to provide healthcare. We think this is borne out.

When flawed research such as the recent PACE Trial is published then it is no longer the case that such a study is accepted without closer scrutiny. The improvement in information technology and the spread of social networking has allowed a better-informed patient base to question seriously the research, and the motives of researchers. When a study purporting to be researching ME does not achieve a single useful function then it is now the patients themselves who can critique such a study and articulate on the poor research as well as the waste of money.

Patients are now empowered and will not accept mediocrity and prejudice in research. It only remains for the media to realise what a scandal has been occurring and for politicians then to force through good science via policy change. The government and the media have a lot of catching up to do. **Listen to the patients** is still a maxim to which healthcare providers, politicians and the media should pay heed.

Continued page 4

Disclaimer

The views expressed in this Journal by contributors and others do not necessarily represent those of Invest in ME. No medical recommendations are given or implied. Patients with any illness are recommended to consult their personal physician at all times.



Diagnosis continues to be at the heart of the problems surrounding ME and diagnostic criteria are critical. One of the liME's aims has continued to be to campaign for such a diagnostic test. Already there is enough research which has identified biomarkers for ME – more awareness of this needs to be given to healthcare providers so that doctors are more easily able to diagnose ME patients correctly.

When Invest in ME started the international biomedical research conferences we were learning of the scientific and political issues that surround ME. We have come a long way since and the publication of a study showing association of XMRV and ME/CFS by Lombardi et al. in the Science magazine in October 2009 has created enormous publicity and interest among scientists who are new to this disease.

The science has been discussed at the highest level of the National Institute for Health (NIH) and in conferences and workshops around the world. A USA blood working group was set up and countries around the world have banned patients with the diagnosis of ME/CFS from donating blood.

In the UK the blood donation ban is permanent - the official reason given being that ME is a remitting and relapsing neurological illness and patients need to be protected from further deterioration of their health. This reason was something which most patient organisations ridiculed as preposterous as the nature of ME has been known for many years. The real reason for introducing the ban was, of course, concern for the recipients and for potential contamination of blood supplies.

Over the past decades UK governments have shown complete disdain for any attempts to properly research and treat ME - a policy decision implemented by the negligence of the National Institute for Clinical Excellence (NICE) and by the corruption and bias in policy-making in the Medical Research Council (MRC) which has allowed a gravy-train of continual research funding to be directed only to a lobby of

psychiatrists – culminating recently in the hapless and flawed PACE Trial which typifies the bogus science which has dominated UK research.

In the Republic of Ireland the blood donation ban came into force in August 2010 (although curiously there was no public announcement). The Irish authorities gave the lie to the UK position on blood donations by providing the true reason for a ban

“to protect of the recipient of the blood donation of possible infectious agent”.

The politics regarding this disease have not gone away – something which may be expected when new discoveries are made – though we doubt if the motives behind some of the denial regarding ME and new research is anything to do with good science. Invest in ME directed attention to this issue this year by arranging a pre-conference evening with Dr Ian Gibson and the US journalist Hillary Johnson presenting on **Science, Politics...and ME**. This will be available on the conference DVD from liME.

The liME conference this year will display biomedical research which, in any other context, would be of interest to policy makers and healthcare strategists. Yet the Chief Medical Officer of England continues to uphold what is now becoming a tradition at the Department of Health - namely to ignore proper research and play no role in changing the way ME is treated and perceived.

Invest in ME wrote to the Lancet to invite the editor (someone who publicly declared that ME advocates should be willing to debate the way ME is treated) to attend. At the time of going to press the Lancet had again declined this offer. These are attitudes from the establishment organisations which are typical of the continuing hypocrisy and abdication of responsibility at the heart of healthcare provision in the UK.

Yet the liME conferences do allow a platform

Continued page 5



for the biomedical research which is occurring and which will continue to undermine the apathy and indifference of officials who are paid to ensure adequate healthcare is available to patients.

As patients and carers and advocates we have to do ourselves what others should be doing.

Invest in ME was set up with the objectives of making a change in how ME is perceived and treated in the press, by health departments and by healthcare professionals. We aim to do this by identifying the three key areas to concentrate our efforts on in order to raise funding for biomedical research - education, publicising and lobbying. This will provide the focus and funding to allow biomedical research to be carried out.

Our aim is to bring together like-minded individuals and groups to campaign for research and funding to establish an understanding of the aetiology, pathogenesis and epidemiology of ME – which will lead to the development of a universal diagnostic test that can confirm the presence of ME and, subsequently, medical treatments to cure or alleviate the effects of the disease.

The seriousness of the situation regarding ME makes it necessary for governments to provide "ring-fenced" funding for bio-medical research into ME (as was provided for HIV/AIDS) in order to address the need for development of diagnostic tests and remedial treatments.

We believe governments should standardise on usage of the Canadian Consensus Criteria for diagnosis, so that there is an agreed basis (noting that evolutionary improvement would be welcomed). We believe governments need to not only endorse and adopt the World Health Organisation classification of ME as a neurological illness, as defined by ICD-10-G93.3. They also need to officially promote it underlining that it is completely separate from the psychological illnesses classified under ICD-10-F48. This will provide the unequivocal distinction for this neurological disease and

avoid the sham science which has been allowed to be perpetuated by psychiatrists who wish to maintain their cash-cow of research funding.

We believe that governments should provide a national strategy of biomedical research into ME to produce treatments and cures for this illness.

But failing this we must take action ourselves.

Since the last Invest in ME conference we have been working to initiate an examination and research institute in Norfolk, UK, which would properly diagnose and then research people with ME. The proposal is described later in the Journal. Thanks to the efforts of the liME steering group members and to Dr Ian Gibson, who has been working tirelessly to support this proposal, we have come within one decision of initiating this and creating a unique UK scenario which would have the potential to lead the world.

But the first step toward creating an improved future is developing the ability to envision it.

And so we have to continue to debate, discuss and promote this work to enable others to see the possibilities. We welcome your support.

The people working for and with Invest in ME are advocates of better education regarding ME. In a sense the speakers who present at the conferences are also advocates – often lonely voices who have fought against a biased and corrupted establishment that has treated this disease so poorly. It is no accident that the presenters at the liME conferences are people who have consciences and who work for the benefit of patients.

Annette Whittemore, the president and founder of the Whittemore-Peterson Institute is making our key-note speech *Translating ME/CFS Research into Treatments* to tell us about the future plans of the WPI. Mrs. Whittemore has

Continued page 6



worked tirelessly to bring ME/CFS to the attention of decision makers so that this illness receives the consideration it needs and deserves. Millions of patients are suffering around the world and the ratio of money being spent on this disease and the economic losses it causes is at odds with any scientific, economic or moral viewpoint.

Dr Judy Mikovits, one of the authors of Science study, was presenting here in May 2009 and had to keep this new information secret. She returns to the IiME conference to tell us how the work has progressed at the WPI and provide data regarding living humans who are infected and being treated with various immune modulators, as well as anti-retrovirals.

We have the great pleasure of hearing Professor Geoffrey Burnstock, President of the Autonomic Neuroscience Centre at UCL, London, who is no stranger to being on the wrong side of established views in his long and distinguished career. Professor Burnstock's work has resulted in no fewer than three paradigm shifts, something that is desperately needed in the policies regarding ME/CFS research and management of patients. Professor Burnstock's work on autonomic nervous system and purinergic signalling is immensely important and may be very relevant to ME/CFS and we hope that his work gives inspiration to other scientists and ideas for clinical trials.

The work of Professor James Baraniuk is concerned with looking at proteins in the cerebrospinal fluid of ME/CFS patients. Dr. Baraniuk and his team's current CFS study builds on a previous study where the team discovered some specific proteins in the spinal fluid of CFS and GWI patients. In the current study they will have a larger group of people with and without CFS/GWI and they will look for those and other unique sets of proteins in the spinal fluid and blood using more sensitive equipment. The team's hypothesis is that these specific proteins are seen in the spinal fluid of CFS and Gulf war Illness but not in healthy controls and that those

proteins will help us understand the cause of these conditions.

Dr David Bell's name is familiar to anyone involved in ME/CFS. He was the local doctor in Lyndonville, New York when 214 people, many of them children, fell ill with mystery flu. He has carried on treating patients and performing research ever since. Currently he is involved in research on retroviruses and CFS being performed by Professor Maureen Hanson of Cornell University.

From Norway promising research by cancer researchers from the University of Bergen using Rituximab is indicative of the value of clinical trials for ME. Professor Olav Mella has 30 years of experience in treating cancer patients. After a patient with a diagnosis of ME/CFS developed non- Hodgkins Lymphoma and was treated for it with Rituximab with unexpected resolution of ME/CFS symptoms as well Professor Mella and Dr Fluge initiated a pilot study with 2 other patients. This has led to further clinical trials with larger number of ME/CFS patients.

We welcome Dr Andreas Kogelnik from California, USA, the Medical Director of the Open Medicine Clinic - a community-based research clinic focused on chronic infectious diseases, neuroimmune disease, and immunology. Dr. Kogelnik has published numerous scientific papers and book chapters, is an Editor of Computers in Medicine and Biology, and is a Consulting Assistant Professor at Stanford University. Together with Dr. José Montoya, he was instrumental in the conception, design, and execution of the EVOLVE study - a placebo-controlled, double-blind study of a subset of chronic fatigue syndrome patients with evidence of viral infection.

Dr John Chia has been a regular speaker at Invest in ME conferences. His work on enteroviruses and ME builds on previous research done in the UK by pioneers such as the late Dr John Richardson. Dr Chia works with his

Continued page 7



son Andrew Chia and their aim is to develop drugs to treat enterovirally-induced ME/CFS.

Professor Kenny De Meirleir has also been a regular speaker at Invest in ME conferences. He is the most prolific and experienced ME/CFS researcher in Europe and treats a great number of patients. His work concentrates on the immune system in the gut.

Professors Tom Wileman and Simon Carding are from the University of East Anglia and will be presenting on the possibilities of research into ME using the facilities and expertise in virology and immunology which are present in the Norwich Research Park area and which we hope to utilise in our proposal for a centre for ME.

Dr Wilfried Bieger practises private medicine in Munich, Germany concentrating on neuro-stress illnesses such as burn out, depression, multiple chemical sensitivities (MCS) and CFS. After the Science magazine 2009 research article on XMRV Dr Bieger decided to look for XMRV in German CFS patients and the results of this study will be presented here today.

May is ME Awareness Month and liME have a number of events around the conference which have been organized. Apart from the conference the **Science, Politics ...and ME** pre-conference presentation will provide more awareness of the reasons why good science is inhibited by policy-makers and vested interests. We have an article in the Journal by Margaret Williams which also describes the effect of the UK Science Media Centre.

liME were recently invited to join the All Party Parliamentary Group (APPG) for ME. We have not always felt this body has been useful for improving the situation with regard to ME but we have decided to accept and hopefully influence future events. As a first step we have asked for the chair of the APPG to accept our invitation to meet with researchers on the day before the IIMEC6 conference in the UK parliament. That will now happen. This is a way

for MPs can hear about real science and research.

liME are also organizing a meeting with researchers – our *Corridor Conference* – as much of the good work at conferences and symposiums is carried out in the corridors between lectures. The idea with this meeting is to promote collaboration and coordination of research.

Our Awareness Month campaign slogan is **Burst Our Bubble** – a reference to the isolation which people with ME and their families have to endure caused by misinformation, ignorance and bogus science. Our posters have been distributed around UK (one is on the back cover of the Journal) – see here <http://www.investinme.org/liME%20ME%20Awareness%20Burst%20Our%20Bubble.htm>.

Invest in ME were chosen as Charity of the Month by London Business Matters – the magazine for the London Chamber of Commerce. The charity took out a full page advert in the magazine to raise awareness of the disease.

The ad can be seen in the online version of the magazine here – <http://www.londonbusinessmatters.co.uk/archive/2011-05/index.html#/38/>

At the conference members of the European ME Alliance will also meet to decide on new initiatives across Europe.

Invest in ME wish to thank those individuals who have donated to us to bring about the 6th Invest in ME International ME/CFS Conference 2011. Thank you for your generosity.



We would like to thank the Irish ME Trust for again sponsoring a speaker and for their continued support and cooperation

Continued page 8



For this issue of the Journal we have included some old and some new articles. With the misinformation about the PACE Trial which has been spread by establishment organisations and individuals, motivated by vested interests or ignorance, it is only right that we take articles from our web site which show the fallacy of the bogus science behind PACE.

We have articles from Margaret Williams which show the disquiet behind how the PACE trial was instigated and also how the reporting on the poor results is spun into a positive message with the help of the Science Media Centre. Long time advocate Kevin Short, who famously took NICE to a judicial review regarding their ineffectual Clinical Guidelines for ME, has also written on PACE.

From the USA patient advocate Chris Cairns has contributed our **Letter from America** article. Chris writes an illuminating blog which is mandatory reading for ME patients and others interested in what is really happening under the covers with the announcements, research and decisions being made in USA.

Chirs Snell discusses the research at University of the Pacific which can use peak respiratory exchange ratio to measure post-exertional malaise and aid in identifying ME patients.

There is already a great fund of knowledge available for the healthcare departments, organisations and staff to appreciate the multi-system nature of ME/CFS and the need to stay current with biomedical research data.

The articles in JIiME, a small subset of the information which exists regarding ME, allow some of that to be seen. The research at the conference continues to echo the question of previous years – what would be possible if proper funding were available for a national or international strategy of biomedical research?

At the conference there will be researchers, clinicians, nurses, patient groups and patients, advocates and, we always hope, a sprinkling of as many politicians, journalists and others whom Invest in ME self-fund to allow people to be

exposed to real science.

The IiME conference provides not just a platform for proper, high-quality science – it allows also a platform for the hopes of millions of people around the world.

Enjoy the Journal. Enjoy the conference.

Clinical Trials

Our theme for the conference is Clinical trials for ME – something which is now clearly needed.

A clinical trial is a scientific research study in which patients participate to help physicians find new or better ways of treating patients. Normally a clinical trial tests a new drug or new medical intervention and its ultimate value in the prevention, diagnosis or treatment of a disease, disorder or illness.

Now is the time to start some well controlled clinical trials into ME/CFS. For far too long patients have been left to manage their symptoms as best they can themselves, often left at the mercy of unregulated businesses promising cures at exorbitant costs and severely ill patients in hospital are often made worse rather than better by unhelpful beliefs about the nature of the disease held by healthcare staff. In a recent survey (Wojcik et al., doi:10.1016/j.jpsychores.2011.02.002) 84% of neurologists did not consider ME/CFS as a neurological illness – a finding which, if true, would categorically show how the misinformation and lack of proper education among the medical profession is costing lives. It also shows how inept and incompetent UK governments and medical organisations have been in regulating medical training, and how organisations such as the General Medical Council, the Royal Colleges of Physicians and Child Health have knowingly or unknowingly contributed to the mess around ME – something which benefits psychiatrists who maintain their status and funding but which does not serve patients. The Invest in ME conferences are aimed at correcting this misinformation.

There have been very few controlled clinical

Continued page 9



trials into ME/CFS. The most recent trial, the so called PACE Trial, which tested the efficacy and safety of cognitive behaviour therapy (CBT), graded exercise therapy (GET), adaptive pacing therapy (APT) comparing it to standard medical care (SMC), gained a lot of publicity from the friends of the investigators who control the media misinformation – but it was soundly criticised by most patient groups who have condemned these results as flawed and not fit for purpose for neurological ME/CFS patients.

We need clinical trials to help healthcare professionals make decisions on how to best help their patients and even if causation of this disease is not known the results of such trials can give researchers ideas where to look. Without evidence from clinical trials treatment remains elusive for most patients suffering from this disease.

ME RESEARCH

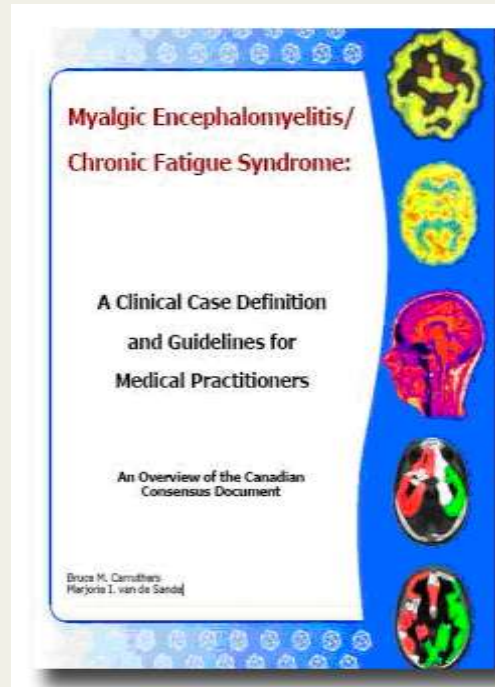
ME press conference September 1990 in San Francisco, with Dr Paul Cheney. Wishing to make sure that the press corps understood how serious a disease ME/CFS is, Cheney continued:

"I think it's really important for members of the press to recognise that what we're talking about here is not common fatigue....What we're talking about here in this systemic illness is that the debilitating fatigue is one of the primary symptoms, as it is in almost all autoimmune diseases and many other systemic diseases....We need to constantly separate out people who have common fatigue from people who have this illness....People who have competent immune systems don't get bad diseases like this in any numbers....Retroviruses have the capacity to impair immune systems in a subtle way".

- "Grey" Information about ME/CFS
<http://tinyurl.com/6xrk9x8>

Canadian Guidelines

Invest in ME are the UK distributors for the Canadian Guidelines. Described even by NICE as "*the most stringent*" guidelines available these are proper, up-to-date clinical guidelines which can also be used as a base for research criteria.



Findings from the study by Leonard A. Jason PhD (Comparing the Fukuda et al. Criteria and the Canadian Case Definition for Chronic Fatigue Syndrome) indicated that the Canadian criteria captured many of the cardiopulmonary and neurological abnormalities, which were not currently assessed by the Fukuda criteria. The Canadian criteria also selected cases with '*less psychiatric co-morbidity, more physical functional impairment, and more fatigue/weakness, neuropsychiatric, and neurological symptoms*' and individuals selected by these criteria were significantly different from psychiatric controls with CFS. The Canadian Guidelines provide a means for clearly diagnosing ME and were developed specifically for that purpose.

They are an internationally accepted set of guidelines for which many in the ME community have been campaigning to be adopted as the standard set of guidelines for diagnosing ME.

Using Cardiopulmonary Exercise Testing to Evaluate Fatigue and Post-Exertional Malaise in ME/CFS

The absence of reliable diagnostic laboratory tests or biomarkers presents significant problems for persons with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), treating physicians, and the ME/CFS research community alike. Typically ME/CFS diagnoses rely on self-report measures where patients describe the extent and duration of their fatigue and attendant symptoms either verbally or on a questionnaire.

An alternative to the current binary approach (i.e., fatigue or no fatigue) or use of paper and pencil inventories for evaluation of symptoms in ME/CFS is to employ direct, objective multi-system, measures of physical function that may also provide insights to the underlying pathophysiology of fatigue in ME/CFS. One such methodology is cardiopulmonary exercise testing (CPET). With a long history of use by exercise physiologists in research settings, this non-invasive, integrative assessment approach is now increasingly endorsed for the clinical evaluation of undiagnosed exercise intolerance and for the objective determination of functional capacity and impairment.[1]

An early definition conceptualizes fatigue as reduced efficiency after doing work.[2] CPET is uniquely able to quantify this reduction in efficiency with measures of both workload and the metabolic cost of that work. Additionally, other available cardiovascular, pulmonary and symptom data further enhance the value of CPET for diagnostic, clinical and research purposes.

As a corollary to extreme fatigue, post-exertional malaise (PEM) or exacerbation of symptoms following physical exertion, is considered one of the most common and recognizable aspects of ME/CFS. For the objective assessment of PEM, CPET has the advantage of serving as both an indicator of clinical status and a quantifiable model of physical exertion.

The principles underlying CPET are simple.

Chris Snell is scientific director of the Pacific Fatigue Laboratory, and chairs the federal Chronic Fatigue Syndrome Advisory Committee (CFSAC). He was one of the presenters at the recent state of knowledge workshop organised by the NIH.

Christopher R. Snell, PhD^{1,2}; Staci R. Stevens, MA²; Todd E. Davenport, DPT, OCS^{2,3}; J. Mark Van Ness, PhD^{1,2}

¹ Department of Sport Sciences, University of the Pacific, 3601 Pacific Avenue, Stockton, CA 95211, USA

² Pacific Fatigue Laboratory, 3601 Pacific Avenue, Stockton, CA 95211, USA

³ Department of Physical Therapy, Thomas J. Long School of Pharmacy and Health Sciences, 3601 Pacific Avenue, Stockton, CA 95211, USA

Physical exertion requires that the cardiovascular system supply oxygen (O₂) to active muscles and the pulmonary system remove carbon dioxide (CO₂) from the blood. Taxing these systems has the capacity to reveal abnormalities that may not be apparent at rest and thus elucidate the mechanisms underlying exercise intolerance in ME/CFS. Procedures for CPET are widely available [1] as are results profiles for a variety of disabling conditions. [3] These data can facilitate differential diagnosis to rule out conditions that could otherwise explain patient symptoms.

CPET is generally performed using a motorized treadmill or stationary cycle ergometer. For reasons of safety, the cycle is preferable when testing ME/CFS patients. Possible orthostatic intolerance and the extreme exhaustion patients usually experience post-testing can make using a treadmill particularly hazardous. Individualized ramp protocols, which involve

Continued page 11

Using Cardiopulmonary Exercise Testing to Evaluate Fatigue and Post-Exertional Malaise in ME/CFS

continued

only modest increases in work rate per stage should be used and tailored to yield a fatigue-limited exercise duration of 8 to 12 minutes. Longer durations may result in patients terminating exercise because of specific muscle fatigue or orthopedic factors rather than cardiopulmonary end points. An important consideration for ME/CFS is to begin the test at a very low workload. Starting at too high a level will make for a very short test with results that are difficult to interpret. Test durations of less than 6 minutes may not show a linear relationship between oxygen consumption and work-rate. [1]

Some of the key measures available from CPET include: maximal aerobic capacity (Peak VO₂ or VO₂ max); ventilatory or anaerobic threshold (VT); and peak respiratory exchange ratio (RER). In addition to these gas exchange variables, workload at any given point and, with the integration of electrocardiography, key indicators of cardiovascular dynamics can also be measured.

Often synonymous with functional capacity or exercise tolerance, Peak VO₂ defines the physiological limits of an individual. However it is important to note that when such terms are used to describe performance on activities like timed-walk tests, or the commercial functional capacity assessments often used to evaluate disability, these are only estimates of aerobic capacity which tend to overpredict VO₂. [1] CPET is required for precise measurement of functional capacity.

Most activities of daily living (ADL) are performed at levels below peak. VT is an important index of submaximal exercise capacity. It denotes the point at which energy production transitions from primarily aerobic to increasingly anaerobic glycolysis and is a crucial measure in CPET as it represents the onset of fatigue. Due to a lack of oxygen in the working muscle cells, work intensity cannot be maintained resulting in the reduction or cessation of activity. It may also be central to

understanding the activity limitations in ME/CFS. If VT occurs at very low levels of oxygen consumption and/or at very low workloads, then even normal ADL may exceed the VT threshold. It is possible therefore that in ME/CFS the increased stress of requiring a greater anaerobic energy contribution even for normal ADL precipitates the symptom exacerbation seen in PEM. CPET provides the only way to non-invasively assess this significant transition point in energy metabolism.

Assessment of subject effort might be considered essential to interpreting any measure of physiological function. Exclusive to expired gas analysis, RER is defined as the ratio between inspired O₂ and expired CO₂. As exercise intensity increases the volume of CO₂ begins to exceed that of O₂. A ratio of CO₂ to O₂ greater than 1.10 is considered an indicator of excellent effort during an exercise test. [1] As an accurate and reliable indication of subject effort, RER substitutes for age-predicted maximal heart-rate values in this respect. Variability of 10-15 beats per minute can be expected within an age group which complicates interpretation of results where percentage of predicted maximal heart rate is the exercise endpoint. [4] There are also difficulties posed by use of pharmacological agents [1] and the cardiovascular abnormalities seen in ME/CFS. [5] Problems of response bias in self-report indicators of effort are also averted.

Because RER permits accurate comparison of subject effort across serial exercise tests, it should be of prime consideration for any clinical intervention trial with functional endpoints. [1] CPET data including RER also allow for the more reliable interpretation of results when an exercise challenge is used to elicit symptoms as part of ME/CFS research studies. As a quantifiable measure of both physiological stress and effort, CPET enables direct comparison between patients and controls on these critical measures. This may be particularly

Continued page 12

Using Cardiopulmonary Exercise Testing to Evaluate Fatigue and Post-Exertional Malaise in ME/CFS

continued

relevant to research looking at immune function where individual fitness levels and exercise intensity can profoundly affect the immune response.[6]

The availability of RER also gives CPET the capacity to objectively document PEM in ME/CFS patients. The reproducibility of both metabolic and work intensity measures obtained through CPET is well documented.[1] But research using CPET to examine functional capacity in CFS has found that a single test may be insufficient to identify abnormalities in work performance among CFS patients.[7, 8] By employing a dual test paradigm (i.e., 2 exercise tests, each separated by 24 hours) it is possible to compare data across tests. A significant change in exercise capacity during follow-up testing with similar peak RER values, it could be argued, is clear evidence of PEM. It should also be noted that RER is a critical arbiter when dealing with accusations of malingering or lack of effort!

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ME FACTS

From over 2,000 pages of information obtained under the Freedom of Information Act, much is already known about the design and progress of the PACE Trial, including the fact that its entry criteria were intentionally broad (*"We chose these broad criteria in order to enhance generalisability and recruitment"*; Trial Identifier 3.6).

Despite the use of such broad entry criteria, there were serious recruitment difficulties, so the entry criteria were broadened even further when on 14th July 2006 Peter White sought approval from the West Midlands MREC to write to GPs imploring them to send anyone with *"chronic fatigue (or synonym)"* for entry into the PACE Trial, thereby opening the trial to anyone who was merely chronically tired.

from Magical Medicine: How to Make a Disease Disappear -
<http://tinyurl.com/38yuj83>

The Media and ME

by Margaret Williams

Margaret Williams is a well respected authority on ME as well as being an ME patient advocate. Margaret Williams formerly held senior clinical posts in the NHS.

Ever since the foundation of the UK Science Media Centre in 1999 – whose purpose is to ensure that the media deliver only headline science stories that accord with Government policies – the reporting of the biomedical science surrounding ME/CFS has been noticeable by its absence. Instead, there has been a wealth of spin promoting the benefits and success of CBT and GET for every disorder imaginable, including ME/CFS.

In plain terms, the Science Media Centre presents only a one-sided view of the available information about ME/CFS, and direct contact with editors and health editors of broadsheet newspapers has revealed their policy of limiting their reporting of ME/CFS to what they receive from the Science Media Centre.

The fanfare of unlimited praise for the PACE Trial results at the press conference held at the Science Media Centre on 17th February 2011 is a case in point, with the media failing to use its critical faculties and regurgitating only what it had been spoon-fed.

There are a staggering number of flaws in the PACE Trial article published in The Lancet (Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Peter D White et al. The Lancet, 18 February 2011 doi:10.1016/S0140-6736(11)60096-2), not one of which was mentioned in the press conference.

These flaws and errors have been identified in a detailed complaint/statistical analysis sent by Professor Malcolm Hooper to The Lancet on 28th March 2011, upon which The Lancet has asked Professor Peter White to comment (a response with which Professor White has apparently not complied within the time allotted for its receipt by The Lancet).

It is understood that under the Elsevier complaints policy, Professor Hooper will be asked to respond to Professor White's reply when it is received by The Lancet; it is also understood that the PACE Trial article was to be sent for re-review by different reviewers and statisticians whilst The Lancet was awaiting Professor White's comments on Professor Hooper's complaint.

There are a staggering number of flaws in the PACE Trial article published in The Lancet

Professor Hooper's analysis will shortly be placed in the public domain; he had agreed with The Lancet to withhold his complaint from publication during the time allotted by The Lancet to Professor White to respond to it, but this agreed time limit has now expired.

There is one crucial point that should not be overlooked amidst the multitude of comments, spin, disquiet and anger surrounding the clearly contrived and exaggerated results of the PACE Trial, which is that if the PACE Trial Investigators had claimed to be studying the effect of CBT/GET on people with medically unexplained or idiosyncratic "fatigue", few people would have objected.

What is fuelling the opprobrium is the fact that

Continued page 14

The Media and ME

continued

the PACE Trial Investigators insist that they have been studying those with "CFS/ME", which is how they refer to the neuroimmune disorder ME/CFS.

The pressing question has to be how the Wessely School can be permitted to disregard the ever-increasing biomedical evidence-base on ME/CFS and to refuse – on no evidence whatever -- to accept the WHO classification of ME/CFS as a neurological disorder.

Some authors have attempted to dismiss this disease as hysterical, but the evidence now makes such a tenet unacceptable....The organic basis is clear

What can be done to halt the Wessely School's anti-science activities and misinformation about ME/CFS which they propagate and disseminate with consummate skill? Since they will not budge from their beliefs, could they be right and the biomedical scientists be wrong? Not at all: the Wessely School is gravely mistaken about the nature of ME/CFS and about their ascription of its symptomatology to a somatoform disorder.

In 1978 (33 years ago), the BMJ published a summary of the symposium on ME held that year at The Royal Society of Medicine:

(BMJ 3rd June 1978)

"there was clear agreement that myalgic encephalomyelitis is a distinct nosological entity. Other terms used to describe the disease were rejected as unsatisfactory for various reasons: the cardinal, clinical features show that the disorder is an encephalomyelitis....Some authors have attempted to dismiss this disease as hysterical, but the evidence now makes such a tenet unacceptable....The organic basis is clear – from the finding that the putative agent can

be transferred to monkeys, the detection of an increased urinary output of creatine, the persistent findings of abnormal lymphocytes in the peripheral blood of some patients, the presence of lymphocytes and increased protein concentration in the cerebrospinal fluid of occasional patients, and the neurological findings"

Apart from their close involvement with the medical and permanent health insurance industry and the unpalatable fact that their professional lives may be shown to have been spent in a null field of research (i.e.. trying to prove that ME/CFS is an aberrant illness belief), it remains a mystery as to why, as bona fide mental health researchers, the Wessely School so persistently refuse to engage with the extensive biomedical evidence-base that exists on ME/CFS.

As Dr David Bell said in his book "Faces of CFS – Case Histories of Chronic Fatigue Syndrome" (Lyndonville, New York, 2000):

"I have no problem with not understanding the exact mechanism of the symptoms of CFS...I do have a problem with the lack of respect given patients with poorly understood neurological disease".

Bell points out that the chest pains, racing pulse, shortness of breath, flushing, trembling, twitching, difficulty maintaining balance, headache, physiological exhaustion to the point of collapse, inability to walk, and pooling of blood on standing experienced by ME/CFS patients all result, not from what Wessely School psychiatrists deem to be deconditioning or "hypervigilance to normal bodily sensations", but from the dysautonomia that is so prevalent in ME/CFS (in an effort to supply blood to the brain, the patient's blood pressure sky-rockets almost to levels that could cause a stroke but then dives,

Continued page 15

The Media and ME

continued

such lability being the easily confirmed hall-mark of classic ME/CFS that was identified many years ago by Dr Melvin Ramsay).

Bell explains that these symptoms are caused by elevation of adrenaline levels that are released in an attempt to compensate for impaired blood flow to the brain due to blood volume deficits and to problems in the blood vessels themselves, which result in the well-known (post-adrenaline-surge) exhaustion: *"(The blood vessels) must be constricted so tight in the brain that little blood gets through. Perhaps it is one of the hormones that constricts blood vessels. Perhaps an infection of the blood vessels. Perhaps it is an excessive sensitivity of the blood vessels to adrenaline....CFS is a devastating physiologic process that undermines the body's energy and the brain's cognitive ability....CFS is not...an illness behaviour for lazy people. The consequences of this illness weigh heavily not only on the victim, but also on family, community and society"*.

ME/CFS is an inflammatory disease (Pasi A et al. Mol Med Report 2011;4(3):535-540). Kennedy et al from the Vascular and Inflammatory Diseases Research Unit at the University of Dundee have reported a whole raft of abnormalities in adults (and subsequently in children) with ME/CFS that are consistent with vascular instability and dysautonomia. These findings include an increase in apoptosis of white blood cells; raised levels of oxidative stress which can damage blood vessels and other organs; increased markers of inflammation, and abnormalities in blood vessel function (Co-Cure RES, MED: 17th May 2010).

Another pressing question must be why the media so frequently fail to report such serious pathology in ME/CFS patients and to rely so unquestioningly on the Science Media Centre to do their work for them. Where is their own intellectual judgment and journalistic skill?

Following the NIH State of the Knowledge Workshop in April 2011, Professor Leonard Jason from DePaul University, Chicago, took part in a televised discussion hosted by Llewellyn King transmitted on 8th April 2011 (The Voice of America, episode #3012) in which Jason said that patients with ME/CFS

"get thrown to the psychiatrists....These are patients who are victimised by an illness and then the media further victimises them, and then the medical community also does it".

Another contributor, author Deborah Waroff from New York, made the point that *"UK patients (with ME/CFS) are probably the most unfortunate in the entire world"*.

Victimisation by the media is well illustrated in the article on the PACE Trial by Adam Morris in The Edinburgh Evening News published on 15th April 2011:

"If implemented, it means patients would be placed on recovery schemes, with thousands benefitting from a new regime of exercise and a 'positive mental attitude' ".

This statement should be compared with the comment by Professor Paul Cheney from the US on graded exercise (made in the UK at the Invest in ME conference in May 2010, proceedings of which are available on DVD from liME – (<http://www.investinme.org/liME%20International%20ME%20Conference%202010%20-%20DVD%20Order.htm>):

"The whole idea that you can take a disease like this and exercise your way to health is foolishness.

It is insane ".

Continued page 16

The Media and ME

continued

Media coverage of ME/CFS remains problematic; comments on the PACE Trial by Vivienne Parry written for the charity AYME (The Association of Young People with ME) published on 14th April 2011 are illustrative.

Ms Parry sits on the Council of the Medical Research Council and was awarded an OBE for services to the public understanding of science. She is on the Board of the Science Media Centre, whose Science Advisory Panel includes Professor Simon Wessely. The Science Media Centre itself states:

"The team at the SMC is advised by a Science Advisory Panel and a Board"

which would seem to indicate a close working relationship between Ms Parry and Professor Wessely.

Ms Parry is described by AYME as a *"highly respected scientific journalist"* but her comments on the PACE Trial do not assist patients with ME/CFS because many of them are inaccurate:

- it is not known *"for sure"* that two treatments (GET and CBT) are *"safe and moderately effective"* for people with ME/CFS because it cannot be certain how many patients with ME/CFS as opposed to *"CFS/ME"* were included in the PACE Trial (*"CFS/ME"* being chronic fatigue in the absence of neurological signs)
- the PACE Trial was not *"as rigorous a study as it is possible to have"*; as a respected scientific journalist, Ms Parry will know that if a trial is not a controlled trial, it cannot be so described
- it is not quite true to say that it was carried out by *"a team of experts"*, since 22 of those carrying out one arm of the trial were trainee psychiatrists employed to work at the Kings College PACE

Centre, London

- APT is not the same as pacing, and pacing was not studied in the PACE Trial
- people with ME/CFS do not have *"fatigue as their main symptom"*; they have post-exertional fatigability accompanied by malaise as their main symptom (their voluntary muscles do not work properly and are exquisitely painful after exercise)
- Ms Parry says: *"There are two problems here. One is about science. Research is about coming up with a hypothesis and then trying to knock it down"*. This is precisely why the PACE Trial cannot be considered *"scientific"*. Although the Investigators' hypothesis that *"CFS/ME"* is exactly the same as ME/CFS and that it is a behavioural disorder reversible by CBT and GET was indeed knocked down by the results, the Investigators refuse to accept that the trial failed

People genuinely cannot understand how individuals who profess to be speaking up for the primacy of science can defend, let alone promote, such a transparently flawed study as the PACE Trial.

- Ms Parry then says: *"Long held, cherished and utterly plausible ideas are regularly demolished by evidence"*. This is true, but Ms Parry fails to understand that the results of both the FINE and PACE Trials demonstrate that the Wessely School's psychosocial model of ME/CFS is wrong and has been demolished by evidence seemingly with no awareness of the paradox in her comments, Ms Parry continues: *"This can be incredibly disappointing but you have to move on and ask the next question, not constantly keep asking the same one in the hope*

Continued page 17

The Media and ME

continued

that eventually you will get a different answer". Refusing to relinquish long held and cherished ideas about the nature of ME/CFS is exactly what the Wessely School have done for the last 25 years, and indeed they continue to do so

- Ms Parry continues: "Some people also said that the trial was meaningless because it excluded those with a neurological disease, therefore could not have contained anyone who had ME since this is a classified neurological disease. This is a bit silly because why would you design a trial that excluded the very patients you wanted to study?"

The answer, Ms Parry, is simple: the Wessely School refuse to accept that ME/CFS is a neurological disorder.

As another, more informed, commentator (JT) has remarked, Ms Parry's article

"is an embarrassment....The trial was not studying the neurological disease ME/CFS but people with chronic fatigue in the absence of neurological signs, or "CFS/ME"....If the Oxford criteria had been applied correctly there would be no people present with ME....People should now be aware that the results were not clinically significant, and there remains little evidence to support the use of CBT and GET in the management of ME/CFS"

Is it not important that highly respected scientific journalists get their facts right and refrain from contributing to the prevailing media bias about which Professor Jason was so outspoken?

People genuinely cannot understand how individuals who profess to be speaking up for the primacy of science can defend, let alone promote, such a transparently flawed study as the PACE Trial.

The failure of CBT/GET is written in the numbers: even the skewed data presented and published in The Lancet show that CBT/GET are of no clinical value in the cohort studied, and certainly do not confirm that the interventions are safe and effective enough to be generalised to everyone with ME/CFS or even "CFS/ME".

ME FACTS

1993: In his now world-famous Testimony before the US FDA Scientific Advisory Committee on 18th February 1993, Dr Paul Cheney said: "I have evaluated over 2,500 cases....We have seen the worst and the best of the range of scenarios that can befall a patient with this disorder. At best, it is a prolonged postviral syndrome with slow recovery or improvement within one to five years. At worst it is a nightmare of increasing disability with both physical and neurocognitive components. The worst cases have both an MS-like and an AIDS-like clinical appearance....We have lost five patients in the last six months....The most difficult thing to treat is the severe pain....The most alarming is the neurological and neurocognitive elements of this disease. Half have abnormal MRI scans, 80% have abnormal SPECT scans, 95% have abnormal cognitive evoked EEG brain maps. Most have abnormal neurologic examinations....40% have impaired cutaneous skin test responses to multiple antigens. Most have evidence of T-cell activation....From an economic standpoint, this disease is a disaster. 80% of the cases evaluated in my clinic are unable to work or attend school...The yearly case production, if plotted, is exponential....The medico-legal aspects of our practice steadily grow as this disease eats at the fabric of our communities. We admit regularly to the hospital (with)...inability to care for self....CFS is an emerging, poorly understood disorder with a distinctive clinical presentation. I am not at all sure that it is as heterogeneous as some would lead you to believe....This disorder is a socio-economic as well as medical catastrophe that will not end....This disease is too complex to rely on standard medical orthodoxy to explain it....Listen to patients with an open mind. Failing that, then listen to those who have spent countless hours with a thousand patients. Most of us have some wisdom to impart and most of that came from patients".

Letter from America

By Chris Cairns

The CFS Patient Advocate



The job of Patient Advocate came upon me uninvited. I did not apply for this job, nor did I have any qualifications for it. I am a sculptor, not a doctor or a researcher. My daughter became sick with a mysterious fatigue illness and I was the obvious person to fill the job. Learning the job of a PA unfolds over time and there is no instruction manual. Certain ideas and thoughts can be transferred from former jobs and former lives, but much has to be learned from scratch. It is helpful in doing the PA job if you have a lot of time and a lot of money, as the solution to this disease takes a great deal of both. It would also be helpful to have an education in bio-chemistry, of which I have none. The most important qualification that a Patient Advocate needs is persistence and discipline. A PA also needs to remain objective and detached, even under the most extreme conditions. Every Patient Advocate has a patient. My patient is my daughter. The objective of this particular Patient Advocate is to make his daughter better. How to set about it is another matter, and turns out to be a complex and sustained set of illusive problems. While most doctors look at a broad and confusing set of symptoms and try to attach treatments to an entire cohort of partially differentiated patients, the PA's problem is slightly different. The Patient Advocate, by job definition, is obliged to help one person - in this case, his daughter - his patient. Thus the PA is looking at one narrow and confusing set of symptoms, which makes his problem slightly easier.

Chris Cairns' blog is at -

<http://cfspatientadvocate.blogspot.com>

A month ago President Obama was asked a question about Chronic Fatigue Syndrome at a news conference. The question came from Courtney Miller, the wife of CFS advocate and patient Robert Miller. For one second, ME/CFS hit the big-time.

Obama answered that he had heard of Chronic Fatigue Syndrome but "did not know much about it". He said that "he would look into it". If Obama has heard of CFS, no doubt it was from Senator Harry Reid of Nevada. If Obama sincerely wants to know more about CFS, he only needs to ask his friend Senator Reid. Senator Reid was instrumental in the formation of the Whittemore Peterson Institute in Reno, Nevada. Senator Reid is the best friend of ME/CFS in the US government. In the last year and a half, the patient voices of ME/CFS have become more spirited, consolidated and articulate. This is a very important development. This elevated collective voice can be seen in many blogs, posts, message boards and advocacy groups. Significant among blogs are those of Mindy Kitei (cfscentral.com) and Jamie Deckoff-Jones (treatingxmr.blogspot.com) and XMRV Global Action Facebook page (<http://www.facebook.com/pages/XMRV-Global-Action/216740433250>). There are many worthy blogs and voices. Forums on phoenixrising.me and mecfsforums.com have many strong and clear voices. To be further convinced of the strength of these patient voices one only need to read the current testimonials of ME/CFS patients that will be presented on May 12, 2011 at the CFSAC conference. All this increased vocal and written activity can be directly attributable to the WPI

Continued page 19

Letter from America

The CFS Patient Advocate

and their effort to find a cause for ME/CFS. The publication in October 2009 of an association of the retrovirus XMRV with ME/CFS ignited a broad and increased interest in this illness. The publication of this fine study stirred great interest, one that went way beyond the particulars of XMRV. The paper was a real jolt - and with ongoing repercussions.

In the past year, Amy Marcus of the Wall Street Journal and David Tuller of the NY Times each have written a series of articles on ME/CFS and on the scientific struggles that surround the association of a retrovirus (or virus) with this illness. In doing this both of them have painted a broader picture of the devastation of this illness. These articles have had nationwide coverage in the United States, and have brought ME/CFS to a higher consciousness for many people. These articles and this coverage of ME/CFS can also be directly attributed to the efforts of the Whittemore Peterson Institute. The October paper has fueled a discussion on the cause or potential cause of CFS/ME that has never been seen before at this level. Lombardi and Mikovits raised the stakes.

Meanwhile the battle over XMRV continues. In the larger picture, XMRV is a detail. The battle really is about another issue - and it is a furious fight to the death. The issue centers on whether ME/CFS is either directly virally induced or an immunological problem that is virally induced. For 25 years there have been great efforts to sink any association of ME/CFS with viruses, (or bacteria, for that matter). Very few people have been looking for such a cause, but very many people have made great efforts to squash any viral cause association. One would have to wonder why? What is the real issue here? It is difficult to comprehend. Do these people just have an individual stake or are there larger forces at work? Why is there so much hostility towards this disease and the patients who suffer

from it? Why is there so little research into the illness and into potential treatments, some of which are currently available?

The recent NIH State of Knowledge conference did very little to advance anything meaningful. A number of government and academic scientists did meet in the same room and exchange ideas - which is always a good idea. However, the NIH meeting itself came to no conclusions, no attempt was made to put the pieces together, *no plan was made for future research to address gaps in our knowledge (as promised in the introduction to the meeting)* and most importantly, no funding for research was proposed. All of this has to be seen as "by design" - or incompetence. More can be read about this on my [blog](http://cfspatientadvocate.blogspot.com),

cfspatientadvocate.blogspot.com, with particular attention to the longer report that was actually not written by me.

One recent positive sign involving the government was the presentation of Dr. A. Martin Lerner at the October 2010 CFSAC Science Day meeting. Dr. Martin Lerner was invited to make a presentation on his treatment data involving antivirals in selected ME/CFS patients. I believe this was the first time that the government sponsored a talk on a potential treatment for a subset of ME/CFS patients. However, neither the HHS nor the CDC has recommended Dr. Lerner's treatment for any patients, continuing their position that there is no known cause for this illness and no known treatments.

While it is clear that the surge in articulating the seriousness of this illness can be attributed to the WPI, Judy Mikovits, Vincent Lombardi, Annette Whittemore and others, this is not to say that important research and treatment are not ongoing in other areas of the United States. Various long-term ME/CFS clinicians have

Continued page 20

Letter from America

The CFS Patient Advocate

continued the struggle to understand this illness and what might work as treatments. Their good work has continued. This includes the practice of Dr. Dan Peterson, who recently made a presentation in Calgary. Dr. Peterson continues to work with some success with the drug Ampligen, as do Dr. Charles Lapp and Dr. Lucinda Bateman. Hemispherx sponsored an important conference on Ampligen in ME/CFS, detailing new studies and attempts to increase efficacy of the drug. Dr. Paul Cheney continues to work on his own treatment protocol, sharing treatment and research ideas with other clinician/researchers, including Dr. Kenny de Meirleir - and also the WPI. Dr. Cheney is doing experimental work with GcMAF and also with Stem Cells. Dr. Joseph Brewer has been working with HIV, ME/CFS and Lyme patients for many years and is interested in new treatment protocols, examining in particular biological associations between CFS and HIV patients, looking for commonalities. Dr. Brewer, too, is interacting with others. Dr. Patricia Salvato has also worked extensively with ME/CFS patients and HIV patients. She, too, is examining a broad treatment protocol based on emerging ideas combined with her vast clinical experience. There certainly are those in the ME/CFS field, including myself, who believe ME/CFS is best characterized or described as "non-HIV AIDS". Dr. Derek Enlander who also has his eyes and ears open to new treatment protocols, is perhaps starting his own Ampligen trial. Dr. Enlander worked closely with Dr. Kerr, until Dr. Kerr was stripped of his academic job and was forced to end his very promising ME/CFS research. Dr. John Chia continues to work with enteroviral involvement in ME/CFS, building his research - with possible new treatments coming in the next couple of years. Several researcher/clinicians have opened their own ME/CFS clinical/research operations. The first is Dr. Jose Montoya at Stanford who runs the Stanford CFS clinic. Dr. Montoya is working on a large study ferreting out the relationship of a host

of pathogens associated with ME/CFS. He is working with Ian Lipkin on this study. Another is Dr. Andreas Kogelnik of Mountain View CA. Dr. Kogelnik will be speaking at the 2011 Invest in ME conference. The third is Nancy Klimas in Miami FL who combines a clinical practice with a research effort that she shares with Mary Ann Fletcher and Broderick Gordon. No systematic framework is in place for these clinician/researchers to work together. No one, except for the WPI, even seems to think about this. For instance the WPI, Dr. Klimas and Dr. Montoya are all working on a cytokine array to identify patients with this illness. No one seems to have an interest in or even an awareness of, what the other is doing. As my daughter characterizes it, ME/CFS is the Wild West of illnesses.

Sparked by this Invest in ME conference, more researchers and clinicians are talking to each other - and exchanging research and treatment possibilities. The positive that can be taken away is that there are many very smart and dedicated people working on this illness - additional candidates to get involved emerged at the NIH State of Knowledge conference, particularly Dr. Michael Dean, and Dr. Theoharis C. Theoharides. We do not want to forget the contributions made by Rich van Konynenburg and his ideas about methylation blockage/glutathione depletion, Dr. Kenny de Meirlier's work with GcMAF, Marian Lemle's hypothesis of H2S involvement in ME/CFS, and Jill Belch's important research at the University of Dundee and the important work being done with Rituxamab in Norway - to mention a few. I apologize to those whom I might have left out. The biggest problem in ME/CFS is the public and "behind the scenes" working of what I would call the "dark force". These are the many people with "black haloes" who want to submerge these ME/CFS patients for the next 25 years - as they have done for the last 25 years. Who are these

Continued page 21

Letter from America

The CFS Patient Advocate

people? They are many, and it would take up too much space to name them. Some are now even dead, to be replaced by new heartless people. Since October 2009 a fresh and resourceful concerted effort is being made to stop all *meaningful* research into the cause or treatment of this illness. This is a continuing phenomenon and again one must ask why?

What is behind this hostility and indifference to a broad and deeply suffering patient population? There are many people who seem to enjoy the negative positions that they can take relative to ME/CFS - and very few who will stick out their necks, and actually try to do something with this illness. Certainly the US government has made it clear that they are not going to directly grapple with this illness. The aggravated, grinding, mean-spirited, indifferent attacks on this illness are ongoing. Does this happen in other diseases? The answer is no, this situation is particular with ME/CFS. Why?

The bottom line is the negative forces have been splendidly successful in blunting any momentum forward with this illness. Great confusions have been generated, with many attendant sideshows of power and ego involvements that are difficult to comprehend. What are the stakes of the game that is being played?

Meanwhile a few patients taking selected antiretroviral drugs show improvements. In talking to Dr. Dale Guyer about a year ago, I mentioned that some patients were going to start taking antiretroviral drugs. Dr. Guyer suggested that he felt these medications certainly might work for a subset of ME/CFS patients, even though one does not know exactly what the drugs are hitting. Dr. Guyer has no problem realizing how sick these patients are.

It has become apparent that the WPI is developing a framework to try a number of

protocols or combo protocols on patients in limited trials. Because of a lack of funding, it is possible that they might just bypass trials and start treating patients and building data. Dr. Judy Mikovits pointed out quite clearly that the WPI was not going to wait another two years to move on to the treatment of these sick patients. They feel that there is a very sick patient population of ME/CFS patients that can clearly be identified. They feel that there are the means by which these patients' immune function can be measured and tracked. They feel that there are treatments to try both on the side of pushing back pathogens and on regulating the immune system. Some of these treatments already exist, some are experimental, and some are coming down the line. From the WPI's perspective, everything is in place to start treating these patients. The WPI is also actively looking for clinicians, researchers and drug companies to help in this effort.

The question now is will the United States government help or hinder the WPI's efforts? All signs right now indicate that the government will hinder the advance of knowledge about ME/CFS. At the end of the NIH State of Knowledge Workshop there was no indication of further plans to accomplish the stated goals of the Workshop: to identify gaps in knowledge and make a plan to solve identified problems. There is also no indication that agencies responsible for health care delivery in the United States have plans to improve the deplorable situation patients face when they try to find a doctor knowledgeable about ME/CFS. Until the U.S. government shows clearly that they are going to address these issues, patients have few choices. We must continue to support those researchers and institutions that are working independently, especially the WPI, who ignited the field in 2009. It is as yet a small spark, but we must nurture it until the causes and treatment of this disease are found.

International Science Symposium on ME

Bond University, Queensland, Australia

3-4 December 2010

Bond University, Queensland, Australia.

The first paper was by **Nancy Klimas (Miami, USA)**, and she presented a systems biology approach to ME/CFS. She described CFS is a disorder of homeostatic imbalance. She briefly outlined her 25 year history of involvement with this illness, when initially she worked on the theory of a chronic immune activation syndrome, with an immunological focus. It was next recognised as a neuro-inflammatory disorder, and now genomics have become involved. She listed and described some of her current research work.

One study involved an exercise challenge to induce relapse, looking at the gene expression and immune changes before, immediately after and 4 hours later. 3 matched groups were studied: Gulf War illness, CFS and controls. The exercise challenge was 8 minutes on an exercycle with measurement of VO2 max. The gene expression showed significant differences in those with GWI and CFS. (By case definition GWI and CFS meet the same criteria). Immunological pathways were similarly affected – these were mainly inflammatory, and the immune cascade led to many symptoms 4 hours later. Symptoms involved the endocrine, immune, autonomic and neurological systems. The genes regulating NK function which included abnormal perforin and granzyme levels were affected.

She then went on to describes Broderick's 3 basic elements of analysis of immune signals, and related this to the states after the 8 minute challenge:

1. Those that looked different
2. Those that hang out with a different crowd
3. Those that behave differently (altered response dynamics)

The International Symposium on ME/CFS was organized by the Alison Hunter Memorial Foundation of Australia and Bond University in Brisbane and held in Brisbane on 3-4 December 2010. Invest in ME sponsored a researcher to the symposium. This was an important meeting and attracted new researchers to the field of ME and we feel this excellent summary by Rosamund Vallings needs to be published again to show the possibilities with research into ME.



Dr Rosamund Vallings from New Zealand is the secretary and newsletter editor of the International Association for Chronic Fatigue Syndrome/ME (IACFSME). Dr Vallings has over three decades of experience in the field of ME/CFS. She has written numerous summaries of medical ME/CFS conferences and meetings from around the world for the benefit of others. In 2008 she was appointed a Member of the New Zealand Order of Merit (MNZM) for services to people with chronic fatigue syndrome (CFS).

In this study there was persistent inflammation, a surge in immune interaction and an IL-1 "splash" effect. There was a huge cascade effect in 8 minutes and persisting 4 hours later. Homeostasis is "messed up" and needs to remodel.

Continued page 23

International Science Symposium on ME

There is a need to focus on autonomic and immune therapies which do interface with each other. This study confirms that graded exercise is not good for those with CFS, and patients must stop exercise well short of the aerobic threshold. Breaks between exercise need to be twice as long as the duration of the exercise.

Hugh Perry (Southampton, UK) discussed the adaptive and maladaptive components of what he describes as "sickness behaviour". He then focused on the language of "sickness" in relation to the way the systems behave during inflammation, for example "feeling ill" with pain and fever. He described sickness behaviour as an organised strategy which is not "bad".

Infection leads to an inflammatory response with release of cytokines, which then communicate with the brain and cause symptoms such as malaise, fever and depression. Systemic inflammation activates selective brain regions, with different challenges activating different regions. This mechanism works through the macrophages in the brain via the blood-brain-barrier. Endothelial cells communicate with the macrophages via the microglia. This is an important part of homeostasis, and is usually transient.

He then went on to talk about chronic neurological disease when microglia increase in number and activation and become "primed". Exaggerated sickness behaviour then occurs in those with chronic brain disease, in response to infection. The microglia release cytokines very readily if already primed. A maladaptive pathway develops.

One study involved the follow up of 300 Alzheimer's disease (AD) patients 2 monthly for 6 months. Those who had an infection had a more rapid mental decline, while those who had suffered no infection showed no change. Other "behaviours" also changed greatly as a result of infection. He described obesity, smoking, age and grey hair as all contributing to earlier AD as all these have inflammatory

effects.

He concluded by saying that systemic infections lead to distortion and maladaptation exhibited by sickness behaviour, because of the primed microglia. This in turn leads to accelerated progression of brain disease. He said that a vaccination can be used as a challenge to demonstrate changes. Functional MRI has more use at detecting these changes.

Mary Ann Fletcher (Miami, Florida) presented her work on biomarkers for CFS. The goal in CFS research has been to find a biomarker or combination of biomarkers. This will enhance the ability to diagnose and demonstrate severity of the illness, define subsets and help to manage trials.

Natural killer (NK) cells were studied initially looking at function and the diminution of perforin and granzyme. 176 CFS patients showed significantly lower function in NK cells compared to controls. She then went on to describe how neuropeptide-Y (NPY) is involved in the stress reaction with increase in norepinephrine and NPY from the sympathetic nerve endings. In a controlled study, NPY was considerably higher in CFS compared to controls.

Use of receiver operating curve (ROC) analysis was described, and this showed discrimination between CFS patients and controls. Using ROC, NPY was found to be 80% sensitive in CFS, (which is better than the PSA test we use to help diagnose cancer of the prostate). NPY also correlates with markers of disease severity. Other potential biomarkers using this technique included 10 of 16 cytokines measured, NK cell function and dipeptidyl peptidase/CD26 which is indicative of immune activation. This is all part of a complex integrated system.

In future exercise challenge will be included in testing this paradigm, and computer analysis will be developed to stimulate research in further clinical trials. These abnormalities may have applications in other diseases.

Continued page 24

International Science Symposium on ME

continued

Dominic O'Donovan, (Cambridge,UK) a neuropathologist presented the results of autopsy on 4 patients who had a specialist diagnosis of CFS:

1. A 32 year old male with a 20 year history of CFS, who died of a suicide overdose of medication. Spinal cord and brain at autopsy showed excess corpora amylacea, which was in excess of normal ageing. There were intermediate filaments closely related to glial cells, and maybe within the glia rather than the axons. No evidence of ganglionitis. (EBV negative)
2. A female of 32 with a 5 year history. She had been unable to tolerate food or water, due to the pain and discomfort of ME/CFS. She finally died of renal failure. The pathology showed a focal chronic inflammatory infiltrate (T8 lymphocytes) in the dorsal root ganglia. (EBV negative).
3. A female of 43 – an assisted suicide in Switzerland with a barbiturate overdose. The brain showed global ischaemia, but this was likely due to the drugs used. Dorsal root ganglia showed mild excess of lymphocytic nodules of nageotte but with no obvious inflammation, but this could represent a subtle chronic inflammatory state.
4. A female of 31 whose death may have been due to opiate ingestion. There was some toxic demyelination with spinal subarachnoid haemorrhage, but she was on warfarin. There was some mild possible chronic ganglionitis.

Differential diagnosis here was discussed and would have included AIDs, Sjorgren's syndrome, varicella zoster and paraneoplastic disease.

These results have raised the possibility that some cases of CFS may have sensory or autonomic ganglionitis. A specific brain and tissue bank in the UK is proposed.

Olga Sukocheva (Adelaide, Australia)

presented the immunohistochemical and microbiological post mortem findings in a 20 year old patient with fatal idiopathic encephalopathy. This patient had been diagnosed with CFS following a severe encephalitic like illness aged 10. There was evidence of inflammatory damage with suppression of microglial cells. Down regulation of ankyrin B was detected in the white matter of the hippocampus. There was no significant difference in ankyrin G. Tests for Coxiella burnetii and Legionella were instituted. C.burnetii antigens were present in astrocytes, and in the microglial cells in the grey matter of the hippocampus. C.burnetii antigen was also found in spleen and liver macrophages, lymphoid tissue, bone marrow, lung and heart tissues. Legionella antigen was not found.

Dan Peterson (Nevada,USA) started his talk with a brief overview of the incidence and effects of CFS in the USA. He then went on to describe research problems, such as the varied definition, heterogeneity of patients, lack of biomarkers, patient self-selection, researcher bias and lack of funding. He described a number of "scientific journeys" undertaken in CFS research. He stressed the importance of the bringing together of the patient, biotechnology, database informatics, genomics and clinical medical guidelines. Diseases can now be defined from a molecular perspective. Networking and collaboration are keys to successful research. There needs to be large-scale clinical data gathering, with international biospecimen collection.

He then went on to discuss the importance of looking at viral infections in CFS. Leukotropic herpes viruses particularly HHV6, HCMV and EBV are among a number of major candidates in CFS. He reported on large studies in which active HHV6 was detected in 28%, HCMV in 29% and EBV in 51%. 10% were co-infected. Active EBV infection significantly correlates with

Continued page 25

International Science Symposium on ME

continued

the presence of auto-antibodies, with antibodies directed at thyroid peroxidase and parietal cells.

Up to 30% of patients may respond to antiviral medication.

Ekua Brenu (Queensland, Australia) had looked at innate and adaptive immunity in CFS. It was postulated that her study could assist in developing biomarkers. The study involved 253 patients and 100 controls. Studies were undertaken at zero and 6 months. Cytotoxic activity of NK cells and CD8+T cells was significantly reduced. Perforin and granzyme activity was reduced. When looking at NK cell phenotypes, CD56 bright cells were significantly diminished. Cytokine secretion from CD4+T cells showed significant elevation of IL-10, IFN- γ and TNF- α . FOXP3 expression was also heightened in the CFS group. Vaso-active intestinal peptide (VIP) receptors were also investigated and found to be significantly elevated.

Kenny de Meirlier (Brussels, Belgium): Because chronic activation of the immune system is present in progressive HIV and is a better predictor of disease outcome than viral load, it is important to test the hypothesis that a similar pattern may be observed in XMRV positive CFS patients. 16 XMRV positive patients (using culture assay) had a large number of tests performed. These patients were found to have reduced lymphocyte numbers and CD-57+lymphocytes reduced, as observed in HIV. There was evidence of an activated innate immune system (increased elastase activity and C4a). sCD14 was significantly higher than expected, and this correlated with plasma lipopolysaccharide (LPS) a proinflammatory component of the gram-negative bacterial envelope. Low stool IgA indicated dysfunctional mucosa-associated lymphomal tissue in XMRV positive patients. Serum IL-8, IL-10, MCP-1 and MIP-1 β are increased and might constitute a biological signature for viral infection.

This all provides supportive evidence for

microbial translocation being part of the pathology of XMRV +ve patients.

He described a Norwegian study of severely disabled CFS patients in which the plasma LPS was elevated in those with a low Karnofsky score. This suggests a leaky gut syndrome. Stool analysis in CFS patients has indicated overgrowth of enterococci, streptococci and fungi with diminished E.Coli count. This can lead to overproduction of hydrogen sulphide which is toxic to mitochondria and affects ATP.

Richard Kwiatek (Adelaide, Australia) is a rheumatologist with a particular interest in neuro-imaging. MRI was performed to look for brainstem dysfunction in CFS. Whole-brain optimised voxel-based volumetry and novel quantification of T1-weighted and T-2 weighted signal levels in structural MRI were used. Voxels build a 3-D map of the brain. In the CFS patients seated pulse pressure was reduced, and seated heart rate and asleep heart rate were increased, compared to controls. This was then correlated with brain change, other symptoms and fatigue.

Prefrontal white matter volume reduced with increasing sleeping heart rate in CFS with the opposite in controls. Midbrain white matter volume reduced with increasing fatigue. There was a strong correlation between total brainstem grey matter volume and seated pulse pressure in the CFS patients. Brainstem grey matter changes suggest a failure of cerebrovascular auto-regulation, potentially mediated by astrocytes. Astrocyte dysfunction may therefore be central to CFS pathogenesis. There seems to be disrupted autonomic nervous system homeostasis. He does not feel it is reduced blood volume that will be causing this.

Barrie Marmion (Adelaide, Australia) has studied Q-fever and its aftermath for many years. There were 11 suffering from post Q-fever fatigue syndrome out of 39 who had had the acute illness in one study cited. The

Continued page 26

International Science Symposium on ME

continued

C.burnetii antigen persists, and causes immune modulation with gene expression and symptoms. Usually it is continuous from the initial onset, but episodic relapses may occur due to re-infection or inadvertent Q-fever vaccination. IL-6 is elevated and IL-2 is down. The symptoms fit the criteria for a diagnosis of CFS.

3 Q-fever groups were studied and there were differences in the frequency of carriage of HLA-DR B1*11 and of IFN- γ . 35% were positive in the post-Q-fever syndrome group, and the levels were low in the controls and Q-fever recovered group and the Q-fever endocarditis group.. These differences support the concept of different immune states in chronic Q fever, determined by genetic variations in host immune responses, rather than by the properties of *C.burnetii*.

Anne Boullerne (Illinois, USA) discussed the issue of chronic fatigue in relation to CFS and MS. She described MS as a characteristic auto-immune disorder. She outlined the differences in incidence, symptoms, duration of illness etc. She emphasised that while MS is a neuro-immune disease, CFS is an acquired severe complex system dysfunction. In MS there is oligoclonal IgG in the CSF in 95% of cases, and brain lesions with T and B cells are seen on MRI. She asks the question "Is gliosis present in CFS?" In CFS MRI abnormalities maybe found such as small punctate subcortical white matter intensities in the frontal lobes, small ventricular volume, slow blood flow and some atrophy. She had looked at functional MRI in relation to control imagery and visual imagery. Both were found to be slower in CFS compared to controls. Changes associated with finger tapping and auditory monitoring correlated with subjective fatigue and brain response during challenge involving memory.

Using M.R.Spectroscopy, there was an increase in choline in the basal ganglia, no significant difference in glutathione, and ventricular lactate was elevated. There was no alteration in levels of GABA and glutamate.

In a rat model for Gulf War Syndrome, using pyridostigmine, there was no gliosis and no increased permeability of the blood brain barrier.

A possible auto-immunity including vasoactive neuropeptides is hypothesised.

Warren Tate (Dunedin, NZ) and his team have just initiated a study to develop tools that can accurately detect molecular changes within cells in response to double-stranded RNA (dsRNA) relevant to CFS. He explained how recent XMRV findings had stimulated research and a need for a bank of genetic material. Biomarkers need to be established as well as less specific markers to reflect changes in global homeostasis. There needs to be targetting of a vulnerable point in the biology of XMRV viral RNA that determines the ratio of its structural and enzyme proteins.

He went on to describe types of biomarkers:

1. Specific such as in a cell undergoing apoptosis: RNaseL, PKR, phosphorylation of PKR etc
2. Specific biomarkers of disturbed homeostasis
3. General biomarkers – marking global disturbed homeostasis of various organs

He explained the RNaseL activation pathway. RNaseL cleavage may be specific to CFS. He is currently studying the ratio of the RNaseL terminal fragment to uncleaved protein. He will also be looking at abnormal PKR activation. This is cleaved by caspase to form the 37D fragment. This undergoes phosphorylation which can be measured – the protein-synthesis factor e1F2a. These 2 phosphorylation events will be detected by specific antibodies against the phosphopeptides of the 2 proteins.

Douglas Feinstein (Illinois, Chicago) presented study of noradrenergic treatments for neuro-degenerative diseases. Glial cells are activated producing neurotoxins, which

Continued page 27

International Science Symposium on ME

continued

induce neuronal damage and leukocyte infiltration into the CNS. Noradrenaline regulates glial inflammatory responses, exerts neuroprotective effects and helps maintain the integrity of the blood brain barrier (BBB). Dysregulation of noradrenaline signalling could exacerbate disease. The supposed reductions of noradrenaline increase inflammatory responses, the amyloid burden and neurotropic factors. Noradrenaline is mainly produced in the locus coeruleus (LC). This part of the brain is damaged in Alzheimer's and Parkinsonism. LC loss correlates with plaque and tangle numbers. The question was asked "does increasing noradrenaline in the CNS improve things?" The drug Droxidopa is a precursor of noradrenaline. This drug is in phase 3 trials for neurogenic orthostatic hypotension. In mice the drug leads to improvement in plaques and learning. This drug used in MS and experimental autoimmune encephalomyelitis (EAE) showed stabilisation compared to controls. This trial indicates that the LC is significantly damaged in MS and EAE.

Noradrenaline directed therapies need to be considered if there is perhaps also LC disturbance in CFS.

Doina Ganea (Philadelphia, USA) spoke about Vasoactive Intestinal Peptide (VIP) – an endogenous and exogenous immunomodulator. VIP downregulates the innate immune response by inhibiting the release of pro-inflammatory cytokines, chemokines and nitric oxide by activated macrophages, microglia and dendritic cells. It also affects the adaptive immune response by reducing the co-stimulatory capacity of antigen-presenting cells, and by inducing Th2 type responses. She had looked at several diseases, such as collagen-induced arthritis and autoimmune encephalomyelitis. She had used dendritic cells generated in the presence of VIP/PACAP as immunomodulatory agents, with positive results.

Monica Carson (California, USA) had studied the CNS expression of the classic chemokine

CCL21. This is a predisposing factor for auto-immunity due to the proliferation induced pre-activation. It thus contributes to chronic inflammatory disease and auto-immunity. Experimental work was done using mice. Resulting data indicated that CCL21 expression within the CNS has the potential to contribute to T-cell mediated CNS pathology. This could occur via homeostatic priming of CD4+T cell lymphocytes outside the CNS, and CD4+T cell migration into parenchymal site after infection with organisms such as toxoplasma.

Donald Staines (Gold Coast, Australia)

rounded off the formal papers with a presentation looking at novel treatments in CFS. He considered whether auto-immunity affecting vaso-active neuropeptides suggest a pathomechanism. ME/CFS may be associated with auto-immunity affecting the function of vaso-active neuropeptides, such as VIP and PACAP (pituitary adenylate cyclase activating peptide). Upsets in adenylate cyclase (AC) signalling and cAMP functioning possibly involving ATP toxicity may be a feature of VN auto-immunity. Purinergic receptors such as ATP negatively regulate AC. He outlined some basic biochemical principles to clarify things; AC amplifies incoming intracellular signals; PACAP is an acetylcholine co-transmitter; AC is involved in long term potentiation and enhanced maintenance of neuronal activity. VIP/PACAP synergism is involved with potentiation of cardiac firing, anti-apoptosis function, cAMP and insulin control, hypoxia regulation and glutamate metabolism. Purinergic signalling is involved in centrally mediated pain (neuropathic pain).

He then went on to describe some likely treatment possibilities based on these principles. These included purinergic signalling modulators, VIP/PACAP mimics/analogues, phosphodiesterase inhibitors: eg Rolipram (toxic), Ibudilast, Roflumilast; B cell depletors (Rituximab); chondroitinase; VIP liposomes and

Continued page 28

International Science Symposium on ME

continued

lentivirus agents. Some of these could be considered for clinical trials.

DAY 2 – was involved in general discussion with various panels looking at clinical matters, case definition, guidelines and research collaboration. Possible name change was also discussed. There was plenty of open discussion, and being a small group meant an interactive forum with everyone participating.

Some of the salient points:

Name change: most people acknowledged that patients do not find the name CFS describes the severity of the illness – tends to trivialise it. It was agreed that the name ME was more appropriate in many ways, although still not entirely accurate for this illness. There was some discussion as to whether gut symptoms and possible auto-immune activity could be incorporated.

Case Definition: The Fukuda definition is still useful for research and one must bear in mind that many previous studies have used this definition so it should not be entirely abandoned, although all agreed that the Canadian consensus definition is more suitable for clinical diagnosis, and should generally be adopted. It is hoped that this definition will be adopted internationally and renamed accordingly. All agreed that the CDC empirical definition should not be used. The issue brought up earlier at this symposium of “sickness behaviour” as terminology was thought to be a backward step, and would be unpopular with patients, although Hugh Perry explained his reasoning very clearly.

Diagnosis: The importance of biomarkers was reiterated. These need to be user friendly and readily available. There should be opportunity to sub-group according to type of onset, symptoms and gene expression. Clinicians new to this illness need to be aware of the range of longterm diagnoses that may emerge in those with CFS, so that regular ongoing surveillance is important. Uniform assessment tools should be

encouraged, although it is acknowledged that not all types of testing will be available everywhere.

Management/guidelines: Guidelines need to be unified, and there should be collaboration among those working on guidelines. Nancy Klimas stressed that financial assistance should be available for a face to face meeting among experts to work on this.

There was some discussion about the importance of off-label prescribing, as many clinicians feel uncomfortable if they do not stick to evidence based medicine. A recommendation should go out in support of being able to use medication in this illness, where there is some useful research backup, even if not formally trialled, so that practitioners do not need to fear litigation. A longitudinal “n of one” trial of a treatment approach on one patient should be deemed useful, and clinicians should be encouraged to do this and write up their results.

Clinical overview: 5 clinicians presented their views on management, and there was much discussion contributed from those on the floor also. Mieke van Driel (Queensland, Australia) presented an overview of drugs used in CFS. Few trials have been done, and those that have showed little benefit. She recommended that we should let patients guide the research agenda by teaching us what works for them.

Don Lewis (Melbourne, Australia) discussed the importance of food intolerances, and emphasised that although gut symptoms maybe prominent, they may not always occur. A strong family history of intolerances is relevant. He firmly believes that intestinal dysbiosis occurs in almost all his patients and the hydrogen sulphide test was positive in 85% of patients. IgG antibodies were found to many different foods. He now proposes formal laboratory based clinical trials.

Bill Cassimatis (Queensland, Australia) has a number of CFS patients in his general practice and he outlined his general approach. He

Continued page 29

International Science Symposium on ME

continued

mentioned that a number of women with this illness seemed to be worse cyclically, confirming that in some women, hormones are involved. This was discussed further by Rosamund Vallings (Auckland, NZ) who uses oestrogen and progesterone often in women with CFS with cyclical or post menopausal symptoms. Nicole Phillips (Melbourne, Australia) who is a psychiatrist pointed out that some women can become depressed on Depo-Provera.

Norman Hohl (Southport, Australia) is relatively new to dealing with this illness, but as a travel medicine consultant and qualifications in infectious diseases, he has a strong interest in preventative strategies.

Research directions: All agreed that this symposium will lead to collaboration internationally. International concurrent trials are needed, and more funding is essential. Larger worldwide studies are likely to increase funding availability. Collection of observational data can be of value. The idea of establishing a CFS registry was considered a valuable approach although this could be often difficult and time consuming for medical practitioners. Using internet self report will not necessarily generate patients fitting diagnostic criteria. Diagnosis needs to be made with face to face encounter by physicians familiar with the illness. More medical education is thus a very important issue to be addressed.

Immediate plan: A formal press statement was produced for distribution after the symposium outlining the salient points raised. A list of future directions was also formulated. Some further e-mail discussion and collaboration between the scientists and clinicians is envisaged, and this was a very positive outcome from this symposium. Many of these people were new to CFS and had never met before, and it seems a whole new set of directions for future research will ensue.

Those who had presented papers were encouraged to make the full paper available for the website which will be set up and

meanwhile the abstracts will be available.

Christine Hunter and her AHMF team were formally thanked, together with the team from Bond University. Without all the dedication and hard work by all of these people, this symposium would never have been possible, and everyone agreed it was an enormous success. The event had been ably chaired by Prof Ken Donald and Prof Mel Miller.

I would like to thank the Alison Hunter Memorial Foundation and ANZMES for enabling me to attend.

ME QUOTES

"...there is a chronic inflammation, neuro-inflammation, and it upsets the whole balance of your systems...the patients become terribly ill.... The immune system is really cranked up; it's a tremendous amount of inflammation. I think that if doctors could get this in their heads that it's sort of like lupus or one of these really inflammatory disorders...it is that level of inflammation. There's a tremendous amount of inflammatory stuff going on, and there's a lot of inflammation in the brain itself"

(<http://www.litemiami.com/spotlite/index.aspx>) [Also see Invest in ME International ME/CFS Conference 2010 DVD]

The evidence of inflammation in people with ME/CFS is important because the incremental aerobic exercise recommended by the Wessely School and encapsulated in NICE's Clinical Guideline 53 is contra-indicated in cases of inflamed and damaged tissue and inevitably results in post-exertional relapse with malaise, which is the cardinal symptom of ME/CFS.

- Knowledge or Belief

<http://www.investinme.org/Article413%20Knowledge%20or%20Belief.htm>

A UK Centre for Biomedical Research into ME

Invest in ME's outline proposal

At the 5th Invest in ME International ME/CFS Conference in London in May 2010 Invest in ME announced that we had entered into discussions with the University of East Anglia to instigate a research facility for ME. Discussions continued after the conference and we decided to publicise our attempt to set up this facility.

Below is a summary of information relating to a proposal which was formulated by an Invest in ME steering group that was formed to oversee the setting up of this facility.

BACKGROUND

People with ME need early and correct diagnosis, proper treatment and advice. The current status of services for people with ME and their families in the UK is poor with little knowledge of current biomedical research being applied and possible treatments not being made available to patients or healthcare staff. This has resulted in ME patients having no service and there being little progress in attracting new researchers or clinicians to study the disease.

The dangers for people with ME of having no proper clinical examination and no access to possible treatments is that the disease can develop into more severe forms with significant loss of functioning. There is also the danger of mis- or missed diagnosis – a common problem with people thought to suffer from ME.

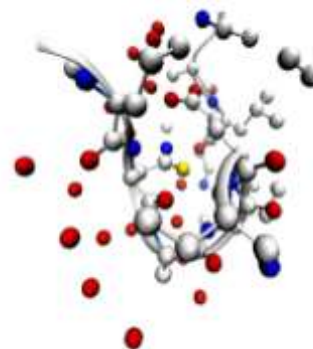
THE AIMS and OBJECTIVES

After five years of campaigning for awareness and promoting better education about ME/CFS the charity felt that the best way to make progress is to establish a national centre of excellence for ME.

The Invest in ME Steering Group (ISG) was formed - consisting of carers of people with ME - to begin work on establishing a facility leading to a UK Centre of Excellence for Biomedical Research into ME.

The ISG believe that a change needs to be

made in the way service provision for ME patients is carried out and is suggesting a simple but effective structure for providing services and instituting major biomedical research into this disease which will have profound effects on the way ME/CFS is treated in the UK and establish a hub of scientific and clinical excellence for ME within Europe.



THE PROPOSAL

The ISG propose for a facility to be instigated with four main elements for diagnosis, treatment and research into ME/CFS – service commissioning, service provision with clinical diagnosis and examinations, translational biomedical research and a research database to allow for more research and improved training of healthcare staff.

Figure 1 shows the elements of the model with patient care and treatment at the centre of the model.

The proposal would be located around the Norwich Research Park in Norfolk. This area contains world-class facilities with a leading university (the University of East Anglia (UEA)), leading research institutes and a modern university hospital (the Norfolk and Norwich University Hospital) - all of which complement the necessary biomedical research which would take place.

Service Commissioning

Service commissioning would be performed by the local PCT. The service would require early and correct diagnosis, examination and

Continued page 31

A UK Centre for Biomedical Research into ME

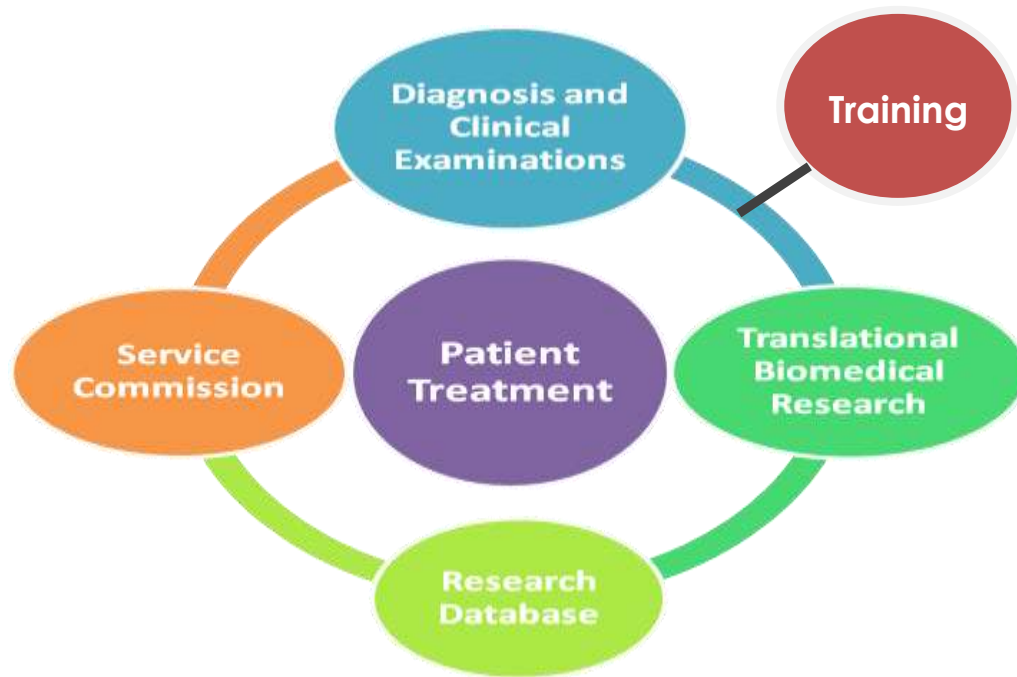


Figure 1

treatment of ME/CFS using a clinical biomedical lead consultant with GPs with special interest being connected to the service.

Diagnosis and Clinical Examinations

The examinations of people with ME/CFS would be commissioned by the PCT. Referrals to the university hospital would be via existing methods from GPs. An important issue is for early and correct diagnosis to be determined. The service would include a clinical biomedical lead consultant who would perform correct diagnosis (using the international standard Canadian Consensus Guidelines), perform a full examination using a standard clinical protocol and, once patients have been formally diagnosed as having ME, administer possible treatments and participate in biomedical research into the disease.

Using a standard diagnostic and clinical protocol the service would allow a model of care and appropriate care packages for people with severe presentations and would establish and co-ordinate a clinical network and disseminate best practice across that

network.

Follow-up examinations would be scheduled so that patients are provided with a service and possible treatments and results from any treatments would be fed back into a database which is administered between the university hospital and the university research faculty. GPs in the area with a special interest in ME would be used to assist and be trained in proper diagnosis and treatment of ME.

Translational Biomedical Research

A parallel but complementary element will be for translational biomedical research to be started by the university in association with other complementary research organisations. The university would undertake biomedical research into ME using cohorts of patients from those being examined at the university hospital and provide possible recommendations for treatment.

The university research would be used for more rapid provision of possible treatments for

Continued page 32

A UK Centre for Biomedical Research into ME

patients whilst at the same time building up the research database for ME/CFS and allowing fostering of new areas of cooperation with other biomedical research facilities.

The research being proposed at the university would be of the most advanced possible – using virology and immunology as the key for examining patients. An important aspect of the biomedical research is that properly defined and distinct patient cohorts are defined and maintained.

The research would be oriented toward translational biomedical research, which allows results from research to be applied toward treatments for ME patients.

The initial proposal for research would aim to initiate studies using the TGAC genome sequencing facility at the Norwich Research Park which would allow all viruses present to be identified in a cohort of well defined patients.

Allied to this would be biomedical research projects – the first of which would examine the possible link between ME and gut inflammation.

A Research Database

These initial and ongoing projects would enable a database to be established for use in further research. This research database will assist epidemiological studies, enhance research potential and provide patients with proper records of treatment.

A research protocol will be established to outline all the study procedures, including data collection and planned data analysis.

THE CURRENT INFRASTRUCTURE

This proposal would make use of the existing infrastructure where patients are initially seen by GPs and referred to a consultant.

Where it differs is that a specialist biomedical clinical lead would be used to perform diagnosis and provide treatment and would be working with a translational biomedical research facility at the university in order to deliver real improvement in patient care from scientific discovery.

THE BENEFITS

Proper examination and treatment benefits patients, their families and the PCT by ensuring that adequate services are provisioned for people suffering from this disease. The hospital and associated staff will be able to be educated in the latest knowledge regarding this disease and would therefore be able to make better decisions. The research proposal would establish this as the most advanced facility in Europe, thus bring more potential for investment and publicity.

The above proposal would lead to a facility with the following benefits –

- * early and correct diagnosis of ME/CFS
- * the clinical lead consultant would assess and plan the development of future services in conjunction with commissioning PCTs
- * it would provide access to specialist assessment, diagnosis and advice on the clinical management, including symptom control and specific interventions, for both patients and health professionals
- * development of a network of local multi-agency domiciliary services to support people who are more severely affected and who are unable to access hospital and primary care services
- * eventual provision of an ambulatory service and/or tele-medical services for those severely ill patients who cannot be moved
- * allow ME/CFS patients (including those severely affected) to participate in clinical trials, where novel research will be conducted, and where medical students can learn about this disease
- * facilitate training and education opportunities for healthcare staff to enhance their knowledge and skills in the diagnosis and management of CFS/ME
- * lead the development of services within primary and secondary care and support GPs and other health professionals in the care of patients with ME.

Continued page 33

A UK Centre for Biomedical Research into ME

- * Allow healthcare staff to feel more comfortable with the diagnosis of ME/CFS being made
- * undertake comprehensive assessments and provide a care package for each patient to include carer and family support
- * Savings on existing consultant referrals and staff by concentrating ME/CFS examination in one area.

TRAINING of HEALTHCARE STAFF

The need for training in ME/CFS is one of the main areas of interest for the ISG. The proposed model would allow the GP network to have access to up to date information about ME/CFS including data on treatments and prognosis.

Specialist advice for more complex cases across the country could be provided based on referrals from other PCTs. This in turn would complement the research database thus increasing knowledge and awareness of treatments. Models of care and appropriate care could be developed with packages for people with severe presentations.

FUTURE DEVELOPMENTS

This model would be developed in the future with an ambulatory service and/or tele-medical services being employed for those who are too ill to attend the hospital examination.

Phlebotomy services would be provided for home visits to be made to allow the severely affected to participate in the research and allow treatments for these disenfranchised patients.

We would seek to establish additional biomedical research projects to be undertaken by the university which would increase the knowledge about the disease and facilitate development of treatments for patients.

In partnership with the charity more training courses would be arranged with visiting experts (researchers and clinicians) being able to share experiences and data and facilitate more education about the disease.

Future developments would see the potential of referrals from other areas (and other countries)

to be created thus generating income and helping to establish the translational research and treatment facility as the foremost facility in Europe for treating myalgic encephalomyelitis.

CHARITY SUPPORT

Invest in ME are supporters of the Whittemore-Peterson Institute (WPI) of Nevada, USA, and have funded UK research by WPI. The WPI have expressed their support for the charity's efforts in establishing a translational biomedical research base in Norwich and have agreed to cooperate. The charity also has European connections and links to other researchers and institutes in Europe and Australia. Our aim is to facilitate collaboration on biomedical research into ME.

The foundations are therefore already in place to advance science and provide the promise of better treatment and possible restoration of function and lives back to a section of the community who have received very little help in the past.

HOW TO LEARN MORE

Contact Invest in ME at info@investinme.org.

SUPPORT US

Our objective is to establish a UK Centre of Excellence for Biomedical Research into ME. We will continue to campaign for this facility to be established.

We welcome all support. Donations to the Invest in ME Biomedical Research Fund will be used to support the establishment of this facility.



Help us by contributing to the Invest in ME Biomedical Research Fund for ME –

<http://tinyurl.com/ydh6whu>

ME FACTS

In 1969 the World Health Organisation classified ME as a neurological disorder.

In 1978 The Royal Society of Medicine accepted ME as a nosological entity.

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

by Margaret Williams

Following publication of the PACE Trial results and mindful of the fact that the Department for Work and Pensions (DWP) was a co-funder of the trial, it may be salutary to reflect afresh on the involvement of Principal Investigators Professors Peter White and Michael Sharpe and the Director of the Clinical Trials Unit (Professor Simon Wessely) with the DWP.

The extracts below are from recent DWP/Atos Healthcare Training Programmes for medical practitioners carrying out assessments on State benefit claimants with ME/CFS.

They graphically illustrate the pervasive influence of the Wessely School's biased beliefs about ME/CFS at the Department for Work and Pensions and the degree of involvement of Professors White, Sharpe and Wessely (a depth of involvement which may indicate that in setting up the PACE Trial, they were not open-minded clinicians seeking to help patients but rather that the PACE Trial was mounted (to quote an influential expert in appraisal of biases in medical research): -

“not to answer a question, but in order to demonstrate a pre-required answer”

(Why most published research findings are false. J.loannidis; PloS Medicine 2005;2:8:e124 – note that this article by loannidis is the most down-loaded in the journal's history).

MEDICAL SERVICES provided on behalf of the Department for Work and Pensions

Training and Development: Continuing Medical Education Programme: Chronic Fatigue Syndrome – Guidelines for the Disability Analyst
Version 4; April 2009. Updated by Dr Peter Ellis.
Version 1 written by Dr Tony Fisher.

“The authors and Medical Services gratefully acknowledged the contribution of the authors (Professor S

Wessely, Professor PD White and Professor M Aylward) of the enclosed articles and their kind permission to reproduce them in this module. In addition the author would like to express his gratitude to Dr P Dewis for his helpful comments and suggestions”.

For more information on Professor Mansel Aylward and his stance on ME/CFS, see pages 428 ff at <http://www.investinme.org/Article400%20Magical%20Medicine.htm>

Together with (then) Dr Aylward, Dr Peter Dewis from the Disability Living Advisory Board authored the Disability Handbook before Dewis became Chief Medical Officer at UNUMProvident in July 2000 after 16 years at the Department of Social Security (now the DWP). In 2002, Dewis wrote about the patients whose claims management posed difficulties for UNUMProvident; in the company's Report “Trends in Health and Disability”, he stated:

“I have commissioned a number of papers from leaders within the medical profession whose disciplines are particularly relevant to those people...whose claims most frequently pose us difficulties in their management.

“A paper from Michael Sharpe has reviewed the developments, not only in chronic fatigue syndrome, but also the range of disorders where the symptoms experienced by individual patients appear to be out of proportion with the physical findings or objective evidence of disease.

“Mansel Aylward who is Chief Medical Adviser to the Department of (sic) Work and Pensions has set out the current trends in government strategy relating to both health and social security.

Continued page 35

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

"My intention would be for this report to be repeated on an annual basis and so become an authoritative and informative document on the current state of medical thinking on those issues which are of greatest importance to us.

"Dr Lipsedge (and) Dr Sharpe have identified the importance of cognitive behaviour therapy of (sic) influencing the outcome in ...chronic fatigue syndrome. This again represents a challenge in ensuring that people are directed towards this approach".

Thus the interest of the DWP and the insurance industry in ME/CFS is clear: it is a disorder that poses "difficulties" for them, so it seems it must be "eradicated", preferably by those who already work for these agencies. It appears that it is those commercial interests, not the plight of sick people, which are paramount. It also seems that, as part of the triple strategy of the "CFS" clinics and the NICE Clinical Guideline on "CFS/ME", the PACE Trial was the ideal vehicle to remove the "difficulties".

Extracts from the DWP Medical Services Training and Development on Chronic Fatigue Syndrome Guidelines:

"This training has been produced as part of a Continuing Medical Education programme for Health Care Professionals (HCPs) approved by the Department for Work and Pensions Chief Medical Adviser to carry out assessments".

"...it must be remembered that some of the information may not be readily understood without background medical knowledge and an awareness of other training given to Health Care Professionals".

"The series is designed to encourage consistency in our approach to complex conditions, provoke reflection on our own

perception with regard to them, and foster awareness of current medical thinking" (i.e. the Wessely School's thinking).

"Chronic fatigue syndrome (CFS) is a disorder, or group of disorders, which continue to cause considerable difficulties for clinician and disability analyst alike (no mention of difficulties caused to patients). Since the terms 'myalgic encephalomyelitis' and 'post-viral fatigue syndrome' both carry implications relating to causation, the generic term CFS is preferred".

"The purpose of this module is to encourage Health Care Practitioners working in disability analysis to adopt a common approach to this difficult and complex illness".

In the first self-assessment exercise, Medical Services assessors are instructed to read the questions and then tick one of the boxes, one of the questions being: **"Most cases of chronic fatigue [sic] are attributable to abnormal illness behaviour"**. "Chronic fatigue" is not the same as "CFS/ME", but even if applied to "chronic fatigue", this is a Wessely School assertion that is not supported by clinical evidence: when carefully examined and diagnosed, patients with many organic illnesses have chronic fatigue, including patients with cancer, COPD, thyroid disease, multiple sclerosis, Parkinson's Disease, liver disease, TB, and many viral illnesses, none of which disorders can be categorised as "abnormal illness behaviour".

The training programme then presents a case study: "Mrs D is a 42-year old woman. You have been asked to assess her and provide a report for a non-medical decision maker. She has completed a claim form herself, amplifying it with several additional pages of hand-written text and a pamphlet describing features of 'ME' ".

Such loaded wording immediately introduces denigration, disparagement and bias into the

Continued page 36

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

training programme for DWP assessors.

The Guidelines for DWP assessors state that anhedonia (loss of any pleasure/interest in life) is commonly present in CFS, which is erroneous, as it is not present in ME/CFS. In 1991, John Wiley & Sons published "Post-Viral Fatigue Syndrome" edited by Professors Rachel Jenkins and James Mowbray; in her own contribution, Professor Jenkins, a Principal Medical Officer at the Department of Health and Director of the WHO Collaborating Centre for Mental Health at the Institute of Psychiatry, made it clear on page 242 that there is no anhedonia in ME.

The DWP Training Guidelines on CFS continue: "At one end of the scale are the (uncommon) cases where there is a very clear history of the sudden onset of fatigue after a proven viral infection, such as Epstein Barr virus; at the other, cases strongly associated with current or pre-existing psychiatric disorder. **In fact, most patients with CFS will also meet the criteria for a current psychiatric disorder**" (citing Simon Wessely and Trudie Chalder).

"From the point of view of the disability analyst, by the time an individual has reached the stage of requiring a functional assessment the diagnosis is likely to have been in place for some time and behaviour patterns firmly established in the minds of the claimant and his medical attendant".

The claimant's medical attendant may be entirely correct in his/her management, but this implied criticism has long been a feature of the Wessely School's dismissal of "naive" clinicians who do not subscribe to their own beliefs about ME/CFS: for example:

"Suggestible patients with a tendency to somatise will continue to be found among sufferers from diseases with ill-defined symptomatology until doctors learn to deal with them more effectively....It has been shown (by whom?) that some patients have always preferred to receive, and well-meaning

doctors to give, a physical rather than a psychological explanation...such uncritical diagnoses may reinforce maladaptive behaviour" (Old wine in new bottles: neurasthenia and ME. Simon Wessely. Psychological Medicine 1990:20:35-53) and "The prognosis may depend on maladaptive coping strategies and the attitude of the medical profession" (The psychological basis for the treatment of CFS. Wessely S. Pulse of Medicine, 14 December 1991:58).

The DWP Guidelines continue:

"It will almost always be appropriate to assess the claimant's mental state, and in the case of IB PCA (Incapacity Benefit Personal Capability Assessment) and ESA (Employment and Support Allowance), to complete a mental health/function assessment".

"The combination of cognitive behavioural therapy (citing Wessely and Chalder) and graduated exercise (citing Peter White) is at present the mainstay of treatment", "treatments" which have been shown to be ineffective in numerous international reports and in surveys carried out by ME/CFS charities, as well as in the UK FINE and PACE Trials themselves.

The Training Programme then instructs DWP assessors to read only a heavily psychiatrically biased reading list (with no mention of any of the biomedical evidence on ME/CFS), including "Occupational aspects of the management of Chronic Fatigue Syndrome: A National Guideline" (2006) in which Professors White, Sharpe and Chalder were instrumental; the NICE Guideline CG53 (2007) which recommends only CBT/GET as the primary intervention, and the 1996 report on CFS of the DWP Chief Medical Adviser's "Expert Group" which included Dr John LoCascio (Medical Director of UNUMProvident insurance company), Professor Anthony Pinching, Dr Peter White, and Dr Charles Shepherd, (Medical Adviser, ME Association).

Continued page 37

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

This "Expert Group" advised that: "**The Chief Medical Adviser** (at that time, Dr Mansel Aylward) **is very anxious to ensure consistency of medical advice which is based on the prevailing consensus of informed expert opinion on this subject** (ie. on the advice of Simon Wessely, Peter White and Michael Sharpe, again with no mention of the substantial biomedical evidence-base). *"The following interests and disciplines were represented: academic research into CFS, clinical interest in the field (from psychiatry, neurology, infectious diseases and general practice), occupational medicine, the insurance industry...and the Disability Living Allowance Board"*.

Key recommendation of this "Expert Group" were: *"The sooner appropriate management was started, the better the prognosis"* and *"Activity should be increased in a managed, step-wise manner"*.

The "Expert Group" agreed that: "**Recovery should not necessarily be equated as getting back to the same condition as before the illness**" (which seems to be a portender of the PACE Trial results). "Recovery" is defined in The Penguin English Dictionary as *"To regain health after sickness"*, which means restoration of full health after sickness; the term "recovery" is not open to idiosyncratic interpretation by the DWP or its "Expert Group".

The "Expert Group" recommended that its report to the DWP's Chief Medical Adviser should be widely available to all those with an interest in CFS (ie. throughout the NHS).

At the end of the Training Programme, assessors were asked to tick more boxes and informed that *"If the objectives have been achieved, you should have no difficulty in responding correctly"*: one of the tick-box choices was: *"The combination of cognitive behavioural therapy and antidepressants should be the mainstay of treatment"*.

The signed, completed form (together with the person's GMC or NMC registration number)

was to be returned to the "Medical Manager at your Medical Services Centre".

The 2010 version

The Foreword to the DWP Medical Services 2010 version (Training and Development: Chronic Fatigue Syndrome [CFS] and Fibromyalgia Learning Set Continuing Medical Education) states: *"The training has been produced as part of a Continuing Medical Education programme for Health Care Professionals (HCPs) approved by the Department for Work and Pensions to carry out assessments"*.

For the DWP Medical Services to conflate "CFS" and fibromyalgia is in breach of the WHO ICD-10 classification which classifies FM as a separate disorder from "CFS/ME" at M79.

This version is particularly prescriptive and has become even more didactic: it ensures that only one message about ME/CFS and FM (the Wessely School's message) is delivered and received:

"A Learning Set is dedicated to the sharing of team knowledge, and must be conducted using internal sources only. External speakers are not acceptable at these events". (This is knowledge control, which is unacceptable ethically, morally and academically).

"This Learning Set is designed to encourage competency based on the subject of CFS and FM and the functional effect of these conditions on the claimant".

"The learning aims are defined and the 'manager' of the Learning Set is encouraged to ensure that these are kept prominently to the fore-front throughout the event, keeping them in view of all participants".

"The only absolute givens are that the essential

Continued page 38

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

content is adhered to and the Learning Set aims achieved".

There is a requirement to ensure that "verification of the learning aims have been satisfied".

Although nominally a DWP Training and Development Programme for assessors, the DWP Medical Services Guidelines state: "It is also necessary to demonstrate that the outcomes of the Learning Set satisfy the requirements of the Continuing Professional Development Programme for Atos Healthcare".

This sounds disturbingly like cult indoctrination and it is little wonder that so many people with ME/CFS report that their assessment(s) by DWP and Atos-trained assessors are traumatic experiences.

In February 2011, the BMJ published an article by Margaret McCartney about Atos Healthcare (Well enough to work? Increasing numbers of people previously deemed medically unfit to work are being taken off state benefits after assessments by a doctor. BMJ 2011:342:d599).

McCartney's article was enlightening: Atos Healthcare is a "French information technology firm, which is subcontracted to the Department for Work and Pensions to provide work capability assessments. In November last year (2010) Atos announced a three year extension to its contract with the department, worth £300 million, to 'support the UK government's welfare reform agenda'. Atos is the sole contractor....A quick glance at internet discussion forums suggests widespread dissatisfaction from people who have been assessed".

"The adverts for Atos, however, consist of a smiling, badged professional saying, 'Getting home on time has become part of my daily routine'. The lack of on-call duties and the 9-5 office hours were also the major advantage plugged at the evening, where nurses and doctors working for Atos helped to promote joining the company".

From her attendance at an Atos recruitment evening, McCartney reported:

"The message from the recruitment evening was quite clear. We were told: 'You are not in a typical caring role....We don't call them patients...We call them claimants'. Training is provided for each type of benefit examination. Its length...depends on experience but is generally up to five days of classroom training, followed by sessions accompanied by a trainer that are audited afterwards".

"Full time doctors can earn £54,000 as basic salary plus various benefits including private healthcare. Sessional doctors work a minimum of four sessions a week....The application forms for sessional doctors state that '10 DLA domiciliary visits per week would earn £40,211.60 per annum. Five LCWRA cases (limited capacity for work related activity) per session, for six session per week, would earn £62,883.60 per annum".

"From the recruitment evening, it was clear that the medical examination consisted of a computerised form to be filled in by choosing drop-down statements and justifying them".

"Is the current method of assessment fit for purpose? There is a queue of people who think not. 'Citizens Advice Scotland (CAS) is extremely concerned that many clients are being found fit for work...despite often having severe illness and/or disabilities. Our evidence has highlighted the cases of many clients with serious health conditions who have been found fit for work, including those with Parkinson's disease, multiple sclerosis, terminal cancer, bipolar disorder, heart failure (and) strokes'. The report found that clients often 'felt hurried in their assessment and that the healthcare professional was ignoring the answers they were providing to the questions in the assessment. There was a general feeling that the assessor made little eye contact with the claimant and spent most of the assessment entering information into their laptop'. This tallies with the recruitment evening, when it was made clear that efficiency with entering details into the computer system was a stipulation of employment".

"The Department for Work and Pensions says...

Continued page 39

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

"It's unfair to suggest that the system isn't working....If a decision is overturned at appeal, it does not necessarily mean that the original decision was inaccurate...". However, this doesn't really deal with the problem that the healthcare professionals doing the assessment are not...forwarding sufficient evidence to enable reliable decisions".

"At the meeting I asked how it was possible to know the variation in symptoms that a patient may have during a one-off assessment. I was told that this could be 'difficult' but this was....a 'functional assessment' ".

"The Citizens Advice Bureau...wants 'better accuracy' in reports. But how can this be achieved when funding is devolved to Atos with no routine access to detailed specialist or general practice based information and opinion?"

Returning to the DWP's Medical Service 2010, its "Learning Aims" are:

- (i) to define CFS and FM (perhaps more accurately, to "re-define" them as functional disorders)
- (ii) to consider "possible causes and functional effects of these conditions"
- (iii) to "consider current management and treatment guidelines (ie. NICE CG53)
- (iv) to "consider benefit issues in children and adults with CFS or FM" and
- (v) to "consider effects of these conditions on work/occupation and effect of work on these conditions".

"It is essential that the Learning Set achieves its learning aims and covers the essential content....It is recommended that all attendees are reminded of the purpose of the Learning Set, the responsibilities of all those present and the learning aims reinforced".

During training discussions, participants must explore the following factors:

- "Ways in which relevant functional problems can present in a claim" (neither ME/CFS nor FM is a functional disorder)
- "The likely functional effects of CFS and FM"
- "Attitudes amongst the team towards the condition"
- "The claimant's perceptions of their disability and barriers to recovery" (such a "barrier" is cited as belonging to a support group).

"The challenge for the facilitator is to ensure that all participants are engaged and prepared to commit to the consensus conclusions" -- in other words, 100% commitment and absolute adherence to the Wessely School model of "CFS/ME" is obligatory on the part of all DWP/Atos Healthcare assessors dealing with patients with ME/CFS.

Would such indoctrination be part of a training programme to assess those with other classified neurological conditions such as multiple sclerosis or Parkinson's Disease?

These DWP training programmes for assessors are extremely disturbing because, as Jason et al have pointed out in a compelling article looking at kindling as the underlying mechanism for the symptomatology seen in ME/CFS, these patients have evidence of extremely serious pathology (An Aetiological Model for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Neuroscience and Medicine* 2011;2:14-27).

Jason et al posit that kindling occurs when an organism is repeatedly exposed to an initially sub-threshold stimulus resulting in hypersensitivity and spontaneous seizure-like activity, and that in ME/CFS patients, chronically repeated low-intensity stimulation due to an infectious illness might cause kindling of the limbic-hypothalamic-pituitary axis and that, once this system is charged or kindled, it can sustain a high level of arousal with little or no external

Continued page 40

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

stimulus, which in turn could lead to hypocortisolism seen in ME/CFS patients, and that seizure activity may spread to adjacent structures of the limbic-hypothalamic-pituitary axis in the brain, which might be responsible for the varied symptoms that occur in ME/CFS patients.

Jason et al cite impressive supporting evidence, for example, Broderick, Fletcher and Klimas et al

“applied network analysis to cytokines in patients with ME/CFS and healthy controls, and outcomes were consistent with a latent viral infection (ie. attenuated Th1 and Th17 immune responses, an established Th2 inflammatory milieu, and diminished NK cell responsiveness)...Chronic cortisol deficiency can cause over-production of the pro-inflammatory cytokine interleukin-6 (IL-6), which has been associated with symptoms of ME/CFS. Lower cortisol, as well as an over-active sympathetic nervous system, could be responsible for the ejection fraction decreases (fraction of blood pumped out of the ventricles per heartbeat) and lower cardiac output among patients with ME/CFS....Because of the Th2 shift, the body would not have an effective defence against viral or intracellular infections....”.

“Baraniuk et al suggested that patients with ME/CFS had unusual proteins in the cerebrospinal fluid, and the aggregation of these abnormal proteins...could cause small amounts of bleeding in the brain (by) causing small punctures in the blood vessels and then small amounts of blood leak into the brain. Other proteins suggest a protease-antiprotease imbalance, increased free radical production, vasoconstriction of the blood vessels, inflammation, and altered rates of cell suicide. Baraniuk et al suggest that inflammation, haemorrhagic elements, increased cell death, and free radical production could be by-products of damage (by these) abnormally folded proteins impeding blood flow and ultimately puncturing blood vessels in the brain”.

“Biswal, Kunwar and Natelson found significant cerebral blood flow reductions in nearly every region of the brain assessed....Neary et al tested whether patients with ME/CFS have reduced oxygen delivery to the brain during and after exercise challenge. They found that in addition to significant exercise intolerance, patients in comparison to controls (have) reduced prefrontal oxygenation, suggesting altered cerebral oxygenation and blood volume in the brain....Neurotropic viral infections could be responsible for the appearance of lesions in the brain and the presence of focal epileptiform seizure activity”.

Referring to the work of Light et al, Jason notes that *“Light et al maintain that exercise could send a continuous signal of muscle sensory fatigue to the central nervous system causing dysregulation of sympathetic nervous system reflexes....About 90% of the ME/CFS patients could be distinguished from control subjects using just 4 of the genes measured...The researchers concluded that ME/CFS patients might have enhanced sensory signal for fatigue that is increased after exercise. These findings all indicate persistent changes in cell membrane function”.*

Referring to his earlier (2009) work, Jason notes that it: *“suggests that being over-extended and going beyond energy reserves can be an impediment to improving functionality and fatigue levels”* and it concludes that *“specific environmental cues”* may trigger ME/CFS. He is clear: *“We need studies based on systems biology that explain the illness, in combination with more details about the environmental contributors to the illness”.*

None of these proven pathologies can be ascribed to deconditioning or to abnormal illness beliefs that are reversible with cognitive restructuring and aerobic exercise.

Just as Peter Dewis of UNUMprovident sees a challenge in ensuring that people are directed towards the Wessely School's behavioural approach, a far greater challenge faces the

Continued page 41

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

ME/CFS community in directing agencies of State such as the DWP, NICE, the MRC and the NHS away from the Wessely School's inflexible approach to a chronic, inflammatory neuroimmune disorder.

For those involved at the highest level in directing the DWP's policy towards people with ME/CFS to have been the ones involved with the PACE Trial could be seen to indicate an unacceptable level of bias and commercial collusion against extremely sick and vulnerable people for whose disorder there exists an abundant biomedical evidence-base which continues to be systematically ignored by the PACE Trial Principal Investigators and those they advise.



ME QUOTES

*"if you look at the activation markers, they are raised in both CFIDS and acute viral illness....Some individuals...will not be able to turn off that activated state. The agent remains as a constant thorn, forcing the immune system to be activated until the agent is eliminated. **In these individuals, the immune system never returns to a normal resting state. So these people are in a state of chronic immune activation. What is the result of this chronic immune activation? If an activated white cell is doing its duty, it has to be producing a certain number of lymphokines or cytokines that are working to control the agent that is infecting the body. But these cytokines can have side effects....Cytokines affect the brain, the bowel, the muscle, the liver (which one sees in CFIDS. So, increased cytokine activation can affect many different tissues in the body (and) can also cause reactivation of other viruses....This disorder could be controlled by eliminating the causative agent or quieting down the hyperimmune system....There is much clinical information showing that (CFIDS) has often led to other immune diseases....The sequelae...include autoimmune disease and, on some occasions, MS".** - Dr Jay Levy*

ME FACTS

in patients with ME/CFS, CBT/GET has been shown to be counterproductive in many patients. Based on the evaluation of the Belgian Reference Centres, the Belgian Minister of Health officially declared that CBT/GET should not be regarded as a curative therapy for ME/CFS. This evaluation revealed that the exercise capacity/condition of the patients treated had not improved and that the occupational participation had even decreased after CBT/GET. Two large-scale patient surveys in the UK and Norway, and two smaller surveys in Scotland and The Netherlands indicate that CBT/GET aggravates the condition of many ME/CFS patients.

- Chronic fatigue syndrome: Harvey and Wessely's (bio)psychosocial model versus a bio(psychosocial) model based on inflammatory and oxidative and nitrosative stress pathways by Michael Maes and Frank NM Twisk - <http://www.biomedcentral.com/1741-7015/8/35>

PACE is dead, long live PACE?

by Kevin Short

In my view, in relation to the PACE trial into 'Chronic Fatigue Syndrome/Myalgic Encephalomyelitis'[1] (published by The Lancet) and some subsequent supportive publications, it is timely for the scientific community and interested observers to consider three questions and revisit some previously published material for possible answers.

The first question is, just why do certain UK psychiatrists apparently refuse to adhere to WHO disease taxonomy, as per ICD-10-G93.3 neurological ME/PVFS and ICD-10-F.48.0 psychiatric FATIGUE SYNDROME respectively, by erroneously conflating what the WHO and an increasing body of biomedical evidence rightly separate? (That, according to some such psychiatrists, 'CFS/ME' is allegedly and primarily both physical and psychiatric and that most illnesses are comprised of both such primary components is often cited as justification: an unlikely assertion if, for example, applied to lung-cancer or HIV/AIDS. Like cancer and AIDS patients, ME sufferers do not object to secondary/co-morbid psychiatric complications being addressed for what they are. They do however object to primary physical illness being misrepresented and mistreated as psychiatric. Such misrepresentation of primary physical illness in the case of cancer and AIDS would rightly be dismissed as ludicrous by most informed people and ditto should be the case for neurological ME/Postviral Fatigue Syndrome categorised by the WHO in ICD 10, G93.3.).

Perhaps in no small part the answer is to be found in earlier published comment. In this case the 2006 UK Parliamentarian Group on the Scientific Research into ME (GSRME) which, in connection with such psychiatrists' role in advising the UK Department of Work and Pensions (the DWP was one of the major funders of the PACE study) on ME/CFS, cautioned:

"There have been numerous cases where advisors to the DWP have also had consultancy roles in medical insurance companies. Particularly the Company UNUM Provident. Given the vested interest private medical

Kevin Short

Kevin Short is a long-time patient advocate who was instrumental in bringing better education and information to the ME community, including key meetings and research which led to the Gibson Inquiry into ME of 2006. His work has influenced many activities in raising awareness and led indirectly to the liME conferences being initiated, Short, along with Douglas Frazer, forced NICE to a Judicial Review regarding the NICE Clinical Guidelines for ME.

Kevin Short Anglia ME Action April 2011.

insurance companies have in ensuring CFS/ME remain classified as a psychosocial illness there is blatant conflict of interest here. The Group find this to be an area for serious concern and recommends a full investigation of this possibility by the appropriate standards body. It may even be that assessment by a medical „expert“ in a field of high controversy requires a different methodology of benefit assessment.” - GSRME Report, Page 30.

www.erythos.com/gibsoninquiry/index.html

The second question is, how on earth does so much psychiatric 'research' that is poorly-conceived, of questionable-quality and undertaken by investigators with demonstrable conflicts of interest receive so much funding and peer-reviewed journal exposure?

Again, in no small part, perhaps the explanation is to be found in earlier published comment. In this case taken from the introductory summary of Professor Bruce Charlton's 2008 peer-reviewed paper entitled 'Zombie Science – a sinister consequence of evaluating scientific theories purely on the basis of enlightened self-interest':

"Although the classical ideal is that scientific theories are evaluated by a careful teasing-out of their internal logic and external implications, and checking whether these deductions and predictions are in-line-with old and new

Continued page 43

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

observations; the fact that so many vague, dumb or incoherent scientific theories are apparently believed by so many scientists for so many years is suggestive that this ideal does not necessarily reflect real world practice. In the real world it looks more like most scientists are quite willing to pursue wrong ideas for so long as they are rewarded with a better chance of achieving more grants, publications and status."

"The classic account has it that bogus theories should readily be demolished by sceptical (or jealous) competitor scientists. However, in practice even the most conclusive „hatchet jobs“ may fail to kill, or even weaken, phoney hypotheses when they are backed-up with sufficient economic muscle in the form of lavish and sustained funding. And when a branch of science based on phoney theories serves a useful but non-scientific purpose, it may be kept-going indefinitely by continuous transfusions of cash from those whose interests it serves. If this happens, real science expires and a „zombie science“ evolves."

In seeking examples of such 'zombie science', in my opinion, few contenders can match the recent UK PACE trial study by Professor Peter White et al published in The Lancet this February that was rightly, and eruditely, criticised by Professor Malcolm Hooper. Outside of the usual supporters, The Science Media Centre and what many would regard as misinformed converts, PACE is widely viewed as a disgrace: having conflated illness rightly separated by the WHO, having effectively ignored a large body of biomedical evidence, having used unscientific and disingenuous patient selection criteria, and having almost exclusively employed subjective and highly unreliable measurement techniques. See:

<http://www.meactionuk.org.uk/COMPLAINT-to->

[Lancet-re-PAACE.htm](#)

With PACE etc in mind, Professor Charlton's 'Zombie Science' critique paper is well worth reading in full. The reference & link for the full text of the paper is: Professor Bruce Charlton – Zombie Science – a sinister consequence of evaluating scientific theories purely on the basis of enlightened self-interest, Medical Hypotheses (2008) 71 327-329, DOI: 10.1016/j.mehy.2008.05.018:

<http://medicalhypotheses.blogspot.com/2008/07/zombie-science-dead-but-wont-lie-down.html>

If the psychiatrists involved in the PACE trial were serious about science, and genuinely believed ME was maintained by fear of activity and muscle deconditioning as they assert, they would have exclusively used rigorous and internationally accepted patient selection criteria to ensure their study was beyond reproach. They did not. If they were serious about science they would have applied objective assessment criteria to properly informed patients. They did not. In my view, PACE represents a gross abuse of the scientific process and a gross abuse of ME patients. Ditto for much of the largely rhetorical and uncritical literature supportive of PACE that, unlike the many patient protestations such as this article, find their way into the so-called scientific literature. From its inception, PACE was roundly and eruditely criticised as being seriously flawed, that it was publicly funded amounts to a gross abuse of millions of pounds of UK taxpayers' money.

In terms of the real-world clinical setting amongst real-world ME patients, I believe the full scientific evidence-base shows that PACE CBT/GET will ultimately contribute nothing positive[2,3]. It will not improve ME patient function in the medium to long term, if at all,

Continued page 44

The Involvement of the PACE Trial Principal Investigators and the Director of the Clinical Trials Unit with the Department for Work and Pensions

continued

and will eventually be seen by most as having been dead on arrival and a complete waste of money: Zombie therapies based upon Zombie science.

Moreover, I believe that most of the PACE Principal Investigators actually know this. If so, my third question is what then could be the real purpose of PACE? Professor Charlton's following observation seems to me to answer that question perfectly:

"If zombie science is not scientifically-useable – what is its function? In a nutshell, zombie science is supported because it is useful propaganda to be deployed in arenas such as political rhetoric, public administration, management, public relations, marketing and the mass media generally. It persuades, it constructs taboos, it buttresses some kind of rhetorical attempt to shape mass opinion. Indeed, zombie science often comes across in the mass media as being more plausible than real science; and it is precisely the superficial face-plausibility which is the sole and sufficient purpose of zombie science."

In my opinion PACE is an issue for more than just ME patients. It is an affront to British science and to British society.

ENDNOTES:

[1] Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial; PD White et al; published online, The Lancet, February 18, 2011 DOI:10.1016/S0140-6736(11)60096-2.

[2] For example, a recent large scale randomised controlled trial demonstrated exactly that: Núñez M, Fernández-Solà J, Nunez E, Fernandez-Huerta JM, Godás-Sieso T, Gomez-

Gil E. (2011) Health-related quality of life in patients with chronic fatigue syndrome: group cognitive behavioural therapy and graded exercise versus usual treatment. A randomised controlled trial with 1 year of follow-up. Clinical Rheumatology. 2011 Jan 15. (E-publication ahead of print).

[3] As Professor Komaroff rightly stated back in 2006:

"...there are now over 4,000 published studies that show underlying biomedical abnormalities in patients with this illness. It's not an illness that people can simply imagine that they have and it's not a psychological illness. In my view, that debate, which has waged for 20 years, should now be over."

Professor Anthony Komaroff, Harvard Medical School: Speaking at the USA Government CDC (Centers for Disease Control and Prevention) press conference on 3 November 2006:

<http://www.cdc.gov/media/transcripts/t061103.htm>



The Enterovirus Foundation was founded in November 2008 and is a non-profit organisation created to fund research to discover the persistent effects of enteroviruses, to determine the role they play in both acute and chronic disease, and to develop treatments to cure and prevent these diseases.

More details at - www.enterovirusfoundation.org

Chronic Fatigue Syndrome Education in the United States

Testimony on CFS Education to the CFS Advisory Committee - 2009

Improved education regarding ME is at the heart of IiME aims. The poor quality of medical education in UK and the apathy of organizations such as the General Medical Council toward correct education regarding ME also has parallels in USA.

Dr. Kenneth Friedman PhD is an outspoken advocate for better education and also a critic of the way education about ME/CFS is being performed in the USA. His testimony at the CFS Advisory Committee Meeting Friday, October 2009 was applauded by the ME community but it also cost Dr. Friedman. He subsequently lost his position as Associate Professor of Pharmacology & Physiology at University of Medicine and Dentistry of New Jersey due to his continuing stand on improving education in the medical community about ME/CFS.

Testimony for the Chronic Fatigue Syndrome Advisory Committee, Oct 30, 2009
by Kenneth J. Friedman, PhD

Good morning!

My name is Kenneth Friedman and I am a medical school professor. I have been asked by the IACFS/ME to comment upon the status of Chronic Fatigue Syndrome education in the United States.

Comments on the Academic, Medical School Environment

The Director of the Office of Ethics and Compliance of my employer has informed me that my off-campus activities related to CFS which include: testifying before this Committee, serving on this Committee, providing continuing medical education courses, establishing medical student scholarships and assisting with healthcare legislation are not part of my responsibilities as a University Professor.

I am told that I will be punished with a penalty as severe as termination of my employment for these activities. I am not a unique target.

- Colleague Ben Natelson has left the same school.
- A different medical school has refused to permit access to their medical students to discuss CFS or inform them of a medical student scholarship.
- A statewide health care provider, with no physician capable of managing CFS patients, refuses to permit a CFS training session for their physicians.

The failure of the CDC to convince the medical-academic establishment of the legitimacy of CFS, and the urgent need for its treatment, has created this environment.

Comments on Medical Student Education

High ranking officials of medical education have testified before this Committee that they are powerless to control the curriculum of medical schools, and cannot mandate the inclusion of Chronic Fatigue Syndrome in the medical school curriculum.

- Were the CDC to mandate the reporting of CFS to the Federal Government, as it does for other illnesses, the National Board of Medical Examiners would have no choice but to put CFS questions on the National Boards.
- If CFS questions were to appear on National Board licensure examinations, medical schools would have no choice but to include CFS in their curriculum.

I have appeared before this body on two separate occasions arguing for the use of existing student programs within both the NIH and the CDC to rotate medical students through NIH and CDC laboratories. I have

Continued page 46

Chronic Fatigue Syndrome Education in the United States

continued

pleaded for dialogue and feedback on any of my proposals. I have heard nothing.

The only mechanism for medical student education for CFS is the medical student scholarship programs run by patient advocate organizations. We now have programs running in three states. How many scholarship programs must be mounted by state patient advocate groups before the CDC mounts a single, national medical student program?

Comments on Continuing Medical Education for Physicians

To my knowledge, the CDC's on-line continuing medical education CFS course is the only involvement of the federal government in healthcare provider education. Does the CDC honestly believe that sitting in front of a computer screen for a few hours will make a physician capable of diagnosing and treating CFS?

From the CFS Community's perspective, what is the impact of the on-line course on diagnosis and treatment of CFS?

- From Vermont CFIDS Association: There is no increase in the number of physicians who diagnose or treat CFS in this state.
- From New Jersey Chronic Fatigue Syndrome Association: The number of requests for physician referrals to our helpline has not diminished.

Comments on Chronic Fatigue Syndrome Educational Materials

In my opinion, all federal and private sector literature concerning Chronic Fatigue Syndrome is out of date. There is no established mechanism for updating health care provider literature.

Of the available literature, the most authoritative and accepted source of information on Chronic

Fatigue Syndrome is a physician's diagnosis and treatment manual not produced by the Centers for Disease Control, not produced by the National Institutes of Health, but produced by the New Jersey Chronic Fatigue Syndrome Association - [The Consensus Manual for the Primary Care and Management of Chronic Fatigue Syndrome](#).

I ask that this Committee recommend to the U.S. Secretary of Health:

- That a national diagnosis and treatment manual for CFS be created,
- That a panel be formed to write this manual,
- That the Department of Health and Human Services underwrite the expense of producing and distributing this manual.

With regard to the recent Spark! Awareness Campaign and the accompanying [Physicians Toolkit](#), not one patient in the State of Vermont ever saw the patient pamphlet. An incredible waste of money!

Conclusions

The only on-going educational programs for medical students and physicians that involve human contact come from patient advocate groups.

- Patient advocate groups are the current source of educational materials for CFS.
- They rely on the assistance of academicians.
- If academicians are threatened with termination of employment for participating in Chronic Fatigue Syndrome education, there will be no educational programs.

I beg you to consider the magnitude of this problem.

I beg you to undertake a course of remedial action.

Thank-you!

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Annette Whittemore

Annette Whittemore is President and Co-founder of the Whittemore-Peterson Institute in Nevada, USA. She graduated from the University of Nevada and taught children who had neuro-cognitive deficits, like those found in autism, ADD, and learning disabilities.

Annette is the parent of a young adult who was severely affected by CFS. She found that few doctors understood the reasons for her daughter's continuing physical decline and therefore committed her time and resources to bringing attention to the serious nature of neuroimmune diseases and change her community in a positive way. She began this important mission in 1994 by supporting a Think Tank on ME/CFS, led by Dr. Daniel Peterson of Incline Village. In 2004 she and another patient advocate began a medical foundation to support research to find biomarkers of disease and treatments for patients impacted by the HHV-6A virus.

In order to provide solutions for patients and bring new doctors into this field of medicine, Annette and others supported a bill to build a biomedical research center at the University of Nevada with an Institute for Neuro-Immune disease and the Nevada Cancer Institute. Annette founded the Whittemore-Peterson Institute for Neuroimmune Diseases which is built on the medical campus with a mission to serve those with complex neuro-immune diseases such as ME/CFS, viral induced central nervous system dysfunction and fibromyalgia.

As the Founder and President, Annette supports the basic and clinical research programs, recruitment of physicians and support personnel, while also leading fundraising activities.

Researchers at the University of Nevada Medical School have also become collaborators on projects that are vital to our understanding of the immune deficits seen in these patients.

Abstract:

WPI's discovery of a human retrovirus in patients with ME (CFS) is significant and may be life changing for those who are impacted. Although additional studies are necessary to clarify the role of gamma retroviruses in human disease,

WPI remains committed to research that will help define the causes of complex neuro-immune diseases such as ME. Identifying accurate biomarkers of disease and translating this information to better treatments continues to be most important to the WPI.

To insure that there are adequate levels of vital biomedical research the WPI continues to encourage and engage in advocacy at all levels on behalf of those who suffer.

Despite many areas of progress much more still remains to be done to educate the public to the realities of this disease and to remove the barriers that prevent effective patient treatment.

ME FACTS

In 1969: the World Health Organisation classified ME as a neurological disorder.

1978: The Royal Society of Medicine accepted ME as a nosological entity.

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Dr. David Bell

Dr. David Bell graduated from Harvard College and gained an MD degree at Boston University. Post doctoral training in paediatrics was completed with subspecialty training in Paediatric Behaviour and Developmental Disorders. In 1978 he began work at the University of Rochester and then began a private practice in the town of Lyndonville, New York. In 1985 nearly 220 persons became ill with an illness subsequently called chronic fatigue syndrome in the communities surrounding Lyndonville, New York. This illness cluster began a study of the illness which continues today.

Dr. David Bell is the author or co-author of numerous scientific papers on CFS, and, in 2003 was named Chairman of the Advisory Committee for Chronic Fatigue Syndrome of the Department of Health and Human Services. Publications include *A Disease of A Thousand Names*, (1988) and *The Doctor's Guide to Chronic Fatigue Syndrome*, (1990). Dr. Bell is currently performing ME/CFS research into the XMRV retrovirus.

Abstract:

Twenty five Year Follow-up of Adolescent Subjects with ME

David S. Bell MD, FAAP; State University of New York at Buffalo

David E. Bell MPH; Department of Anthropology, State University of New York at Buffalo

Contact Information: dsbellmd@yahoo.com

From 1984 until 1987 an apparent outbreak of Myalgic Encephalomyelitis (ME) occurred in New York State, in a small rural area between Rochester and Buffalo. Two hundred ten persons (sixty one children) were identified during this period, and have been followed for the ensuing twenty-five years. Diagnostic criteria for this outbreak were published in 1988¹ prior to publication of the CDC criteria²; in retrospect this outbreak would fulfil current criteria for ME or for chronic fatigue syndrome (CFS). Early papers showed no connection with Epstein Barr virus infection³, and similarity with Primary Juvenile Fibromyalgia Syndrome⁴. An epidemiologic study showed increased incidence within families and association with drinking unpasteurized milk, this latter finding remaining unexplained⁵. In 1995 a paper documented the health of the adolescent-onset subjects 13 years after onset⁶. In this study, twenty percent were disabled and remained very ill, with the most predictive factor being the severity of illness at onset. The remaining eighty percent considered themselves either "much better" or "recovered". Half of these considered themselves entirely well and the other half had mild to moderate symptoms but were functioning fairly well. This study, published in 1995 helped foster the incorrect conclusion that children with ME recovered at a very high rate.

In the current study emphasis was placed upon disability instruments, thus preventing comparison to the 1995 study. Three subjects had developed malignancy (thyroid cancer, cancer of the cervix, and acute myelocytic leukemia) and were not included in the present study (10.7% of respondents). 25 remaining subjects were the subjects of this study. Instruments used included the SF-36, Pittsburg Sleep Questionnaire, McGill Pain Questionnaire, Bell Ability Scale, Visual Analog Scores for 7 symptoms, Number of Hours of Upright Activity Scale, and the Fisk Fatigue Impact Scale.

Two subjects (2/25 or 8%) had scores on these instruments that were close to control scores and

Continued page 49

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

were considered recovered. Eighteen subjects (18/25 or 72%) had "remitting illness", and five subjects had "persisting illness" (5/25 or 20%). The remainder of the study consisted of characterizing illness severity in the "remitting illness" group and the "persisting illness" group.

All subjects in the persisting illness group were severely disabled and acknowledged their disability. Of surprise was that many subjects in the "remitting illness" group was also disabled yet perceived themselves as doing well. Most in this group had altered lifestyles so that they were able to work part time, or had elected to stay at home as parents. The variations between perceptions of health and scores on disability questionnaires led to the conclusion that the majority of subjects in this 25 year follow up study had "health identity confusion, and that this "health identity confusion" should be considered an anticipated outcome of ME in adolescence."

1. Bell D, Bell K. Chronic fatigue syndrome: diagnostic criteria [Letter]. *Ann Intern Med.* 1988;109:167.
2. Holmes G, Kaplan J, Gantz N, et al. Chronic fatigue syndrome: a working case definition. *Ann Intern Med.* 1988;108:387-9.
3. Bell D, Bell K. Chronic fatigue syndrome in childhood: relation to Epstein-Barr virus. In: Ablashi D, editor. *Epstein-Barr Virus and Human Disease*; 1989. Rome, Italy: Humana Press; 1989. p. 412-7.
4. Bell D, Bell K, Cheney P. Primary Juvenile fibromyalgia syndrome and chronic fatigue syndrome in adolescents. *Clin Inf Dis.* 1994;18(Suppl 1):S21-S3.
5. Bell K, Cookfair D, Bell D, Reese P, Cooper L. Risk factors associated with chronic fatigue syndrome in a cluster of pediatric cases. *Rev Inf Dis.* 1991;13(Suppl 1):S32-8.
6. Bell D, Jordan K, Robinson M. Thirteen-year follow-up of children and adolescents with chronic fatigue syndrome. *Pediatrics.* 2001;107(5):994-8.

Dr. Andreas Kogelnik

Dr. Andreas M. Kogelnik, is the Founding Director of the Open Medicine Institute, a collaborative, community-based translational research institute dedicated to personalized medicine with a human touch while using the latest advances in medicine, informatics, genomics, and biotechnology. The Institute works closely with the Open Medicine Clinic and other clinics to conduct research and apply new knowledge back into clinical practice.

Dr. Kogelnik received his M.D. from Emory University School of Medicine in Atlanta and his Ph.D. in bioengineering/bioinformatics from the Georgia Institute of Technology. Subsequently, he completed his residency in Internal Medicine and a Fellowship in Infectious Diseases at Stanford University and its affiliated hospitals.

Following his clinical training, he remained at Stanford with NIH funding to engage in post-doctoral research in microbiology, immunology and bioinformatics with Dr. Ellen Jo Baron and Dr. Stanley Falkow, where he explored host-response profiles in severely ill patients. Together with Dr. José Montoya, he was instrumental in the conception, design, and execution of the EVOLVE study - a placebo-controlled, double-blind study of a subset of chronic fatigue syndrome patients with evidence of viral infection.

Dr. Kogelnik worked with Dr. Atul Butte in translational informatics to determine patterns that indicated a high risk for adverse events in paediatric patients at Lucille Packard Children's Hospital.

Continued page 50

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

He is the Medical Director of the Open Medicine Clinic - a community-based research clinic focussed on chronic infectious diseases, neuroimmune disease, and immunology. Dr. Kogelnik has published numerous scientific papers and book chapters, is an Editor of Computers in Medicine and Biology, and is a Consulting Assistant Professor at Stanford University.

With the Open Medicine Institute, he has led the formation of CFS and Lyme Registries and Biobanks as well as creating an infrastructure for providers to collect better data and implement clinical trials across a network of sites.

Professor Kenny De Meirleir

Professor De Meirleir is a world renowned researcher of ME/CFS. He is full professor of physiology, pathophysiology and medicine at the Vrije Universiteit Brussel and practices Internal Medicine at Himmunitas Foundation also in Brussels. He has published several hundred peer reviewed articles and is co-author of the book 'Chronic Fatigue Syndrome: a biological approach' and was co-editor of the Journal of Chronic Fatigue Syndrome, and reviewer for more than 10 other medical journals.

Professor De Meirleir was one of four international experts on the panel that developed the Canadian Consensus Document for ME/CFS. He assesses/treats thousands of ME/CFS patients annually and is the most experienced researcher in Europe regarding ME/CFS.

His research activities in ME/CFS 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.

Abstract:

CLINICAL DIAGNOSIS, TREATMENT AND TRIALS OF ME/CFS

Part I : Clinical Diagnosis

In the first part of the presentation relevant data with regards to abnormal laboratory findings in ME/CFS patients will be presented. The intention is to give an overview of the most striking abnormalities with clinical relevance. Results of routine laboratory and of specialized tests are discussed with explanation as how they fit in the pathophysiology of the disorder.

In a majority of patients serum sCD14 is increased and CD57+ lymphocyte numbers are low.

Using different methods XMRV/MLV is detected in a majority of ME/CFS patients and this is significant when compared to the prevalence of this retrovirus in healthy blood donors.

XMRV positive ME/CFS patients show a distinct inflammatory signature based on their cytokine blood levels (De Meirleir et al. 2010 ; Lombardi et al. 2011). Recently we demonstrated that XMRV is present in the gut. In one ME/CFS patient XMRV was recovered from his appendix after he underwent appendectomy.

ME/CFS patients have a Th1 → Th2 shift and show increased H₂S metabolites in the urine. This can be demonstrated by a simple self testing urine kit. A subgroup of ME/CFS patients carries abnormal cell surface proteins, which has negative consequences for ion channel function.

Continued page 51

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Faecal analysis and faecal microbial analysis are very useful in the diagnostic workup. They reveal specific chemical and microbial abnormalities with therapeutic implications.

Part II : Treatment and trials of CFS/ME

Apart from the use of anti-inflammatory drugs or compounds, antioxidants and certain nutraceuticals and based on laboratory test abnormalities, following elements of therapy are

common to the therapy of all ME/CFS patients :

1. individualized diet
2. treatment of dysbiosis (pre-, pro- and antibiotics)
3. use of immunomodulators

In specific ME/CFS subgroups, we use antivirals, antimycotic drugs, antibiotics for zoonoses (ILADS protocols) and other directed at specific opportunistic or other infections.

Professor Tom Wileman

Professor Wileman is Professor of Molecular Virology and Director at the Biomedical Research Centre at the University of East Anglia in Norwich, UK. His previous positions in the UK have included the Head of the Department of Immunology and Pathology at the BBSRC Institute of Animal Health, Pirbright.

He was Assistant Professor at the Department of Medicine at Harvard Medical School in Boston, USA where worked at the Dana Farber Cancer Institute and Beth Israel Hospital. He held investigator awards from the Claudia Adam's Barr Foundation for Cancer Research, the Medical Foundation of the Charles King Trust and was Basil O'Connor Scholar of the March of Dimes Research Foundation.

Prior to that he was SERC NATO Fellow and Fellow of the Parker Francis Pulmonary Research Foundation within the Department of Cell Biology, Washington University Medical School, St Louis.

Professor Simon Carding

Professor Simon Carding Professor of Mucosal Immunology at University of East Anglia and Institute of Food Research. Following his PhD at London he held postdoctoral positions at New York University School of Medicine, New York and at Yale University School of Medicine, New Haven, USA.

He then moved to the University of Pennsylvania, Philadelphia, USA as Assistant and later Associate Professor. He joined University of Leeds as Professor of Molecular Immunology in the Institute of Molecular and Cellular Biology in 1999.

His scientific interests are in understanding how the immune response in the gut functions and in particular, is able to distinguish between the commensal microbes that reside in the gut and environmental microbes that cause disease, and in the mechanisms by which the body's immune system no longer ignores or tolerates commensal gut bacteria and how this leads to immune system activation and inflammatory bowel disease.

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Dr. John Chia

Dr John Chia is an infectious disease specialist, Torrance, California, USA. He has published research ("Chronic fatigue syndrome associated with chronic enterovirus infection of the stomach") on the role of enteroviruses in the aetiology of ME/CFS - an area which has been implicated as one of the causes by a number of studies. There are more than 70 different types of enteroviruses that can affect the central nervous system, heart and muscles, all of which is consistent with the symptoms of ME/CFS. By analysing samples of stomach tissue from patients with CFS, Dr. Chia's team discovered that high levels of these individuals had high levels of enteroviruses in their digestive systems. Dr Chia's research may result in the development of antiviral drugs to treat the debilitating symptoms of ME/CFS.

Abstract: Clinical & Research Experience of Enteroviral Involvement in ME/CFS.

John Chia, Andrew Chia. EV Med Research

A number of infectious agents have been implicated in the pathogenesis of ME/CFS. Emerging evidences suggest that enteroviruses can persist in the tissues of ME/CFS patients after acute infections and may be responsible for the various symptoms. Enteroviruses can cause major epidemics of respiratory, gastrointestinal and non-specific flu-like illnesses and disseminated infections including but not limited to meningoencephalitis, myocarditis, pleurodynia, myositis and hand-foot-mouth diseases. Initial isolation of enteroviruses from patients with acute infections followed by demonstration of persistent viral infection in tissues years after the patients developed chronic symptoms lends support to the pathogenic role of enteroviruses in ME/CFS. Presumptive clinical diagnosis of chronic enterovirus infection requires a high index of suspicion, familiarity with the protean manifestations of acute infections and understanding of chronic viral persistence.

A number of tests can support the clinical diagnosis of chronic enterovirus infection. Significantly elevated neutralizing antibody titer over time suggests persistent immunologic response to specific enterovirus(s) infection in the tissues. In contrast to other types of viremic infections, EV RNA levels in whole blood of ME/CFS patients are extremely low, which likely explain the discrepancy of results reported from different research laboratories over the past two decades. Immunoperoxidase staining for viral protein in the stomach biopsies is more sensitive than the neutralizing antibody test or EV RNA detection, and furthermore, demonstrates the antigens in tissues where viruses are expected to replicate and persist based on the route of transmission. The finding of enteroviral RNA and growth of non-cytopathic viruses from the same tissues support the validity of protein staining. The recent finding of double-stranded RNA(dsRNA) in the stomach tissue supports the mechanism of viral persistence in accessible tissue.

Although there is renewed interest in drug development for enteroviruses, clinical studies are still many years away. Presently available therapy is directed toward the continuing immune responses against persistent viral infection. Intravenous immunoglobulin, given monthly or every few months, can ameliorate inflammatory symptoms in less than 1/3 of adult patients, but may be more effective in pediatric patients or patients with severe myalgia. The combination of alpha and gamma interferon can induce short-term remission in about 45% of ME/CFS patients with debilitating myalgia, but is quite expensive and often poorly tolerated. Oxymatrine or Equilibrant have beneficial effects in 52% of 700 ME/CFS patients, but transient increase in pre-existing symptoms are expected in most of the patients. Dose titration improves tolerance. Cytokine gene expression study during therapy demonstrates an increase of IL12/IL10 ratio in responders but not in non-responders. A decrease of

Continued page 53

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

stainable enteroviral protein and dsRNA is demonstrated in the stomach biopsies of few responders on oxymatrine/Equilibrant therapy.

Previous evidence for enterovirus infection in ME/CFS from over a decade ago has been confirmed and extended in recent studies. Mechanism of viral persistence through the formation of dsRNA is similar to observations in tissue cultures and in animal models. Development of antiviral therapy against enteroviruses needs to be expedited; and the importance of enteroviruses in ME/CFS can be realized with a randomized, placebo-controlled antiviral drug trial.

Dr. James Baraniuk

James N. Baraniuk was born in Alberta, Canada. He earned his honours degree in chemistry and microbiology, medical degree, and unique bachelor's degree in medicine (cardiology) at the University of Manitoba, Winnipeg, Canada. Thereafter, he moved to Akron, OH, USA, for his internship and internal medicine residency at St Thomas Hospital. After another year of internal medicine residency at Duke University Medical Center, Durham, NC, he trained with Dr C.E. Buckley, III, in allergy and clinical immunology. He moved to the laboratory of Dr Michael Kaliner at the National Institute of Allergy and Infectious Diseases, Bethesda, MD, and there began his long-standing collaboration with Dr Kimihiro Ohkubo. After 2 years studying neuropeptides, he joined Dr Peter Barnes' laboratory at the National Heart and Lung Institute, Brompton Hospital, London, UK. Dr Baraniuk returned to Washington, DC, and Georgetown University, where he is currently Associate Professor with Tenure in the Department of Medicine.

(from Georgetown University site <http://explore.georgetown.edu/people/baraniuj/>)

Our research team is examining proteomic (protein) differences between veterans with Gulf War Illness (GWI) and healthy veterans in hopes of learning more about how GWI works. In our first study, we are also looking at differences in genetics, pain sensitivity, muscular, and autonomic nervous system function between GWI vets and healthy vets. Based on current data, we believe that GWI may be related to a certain genotype for an enzyme (carnosine dipeptidase-1) that degrades two of the body's important antioxidants.

Our second project is a treatment study using Carnosine, one of these antioxidants. If this genetic difference does contribute to GWI, then replacement of this antioxidant could provide relief of symptoms.

Finally, we are conducting a Chronic Fatigue Syndrome research study. The CFS study is similar to our GWI study, except that we are also doing lumbar punctures (sometimes called a spinal tap) for the people who participate in this study. We are doing the lumbar puncture procedure for two reasons:

- 1) We believe that increased spinal pressure could be associated with some of the symptoms like recurrent headaches, sleep problems, memory problems, chronic fatigue and pain. For this reason, we measure the spinal fluid pressure during the procedure.
- 2) During a previous study, our research team and our research collaborators discovered some specific proteins in the spinal fluid of CFS and GWI patients. In this study we will have a larger group of people with and without CFS/GWI and will look for those and other unique sets of proteins in the spinal fluid and blood using more sensitive equipment.

Our hypothesis is that these specific proteins are seen in the spinal fluid of CFS and Gulf war Illness but not in healthy controls and that those proteins will help us understand the cause of these conditions.

<http://explore.georgetown.edu/people/baraniuj/?action=viewresearch>

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Dr. Øystein Fluge / Professor Olav Mella

Institute of Medicine, Section of Oncology, University of Bergen, Norway

Dr. Øystein Fluge received medical degree in 1988 at the University of Bergen, and is a specialist in oncology since 2004. He has worked as a Research Fellow with support from the Norwegian Cancer Society and is now chief physician at the Cancer Department, Haukeland University Hospital. Doctoral work emanates from the Surgical Institute and Department of Molecular Biology, University of Bergen.

Professor Olav Mella and researcher Dr Oystein Fluge from University of Bergen, Haukeland University Hospital, department of oncology are currently conducting a clinical trial on B-lymphocyte Depletion Using the Monoclonal Anti-CD20 Antibody Rituximab in Severely Affected Chronic Fatigue Syndrome Patients. This study is based on pilot patient observations, and experience from the prior study KTS-1-2008. The investigators anticipate that severely affected chronic fatigue syndrome patients may benefit from B-cell depletion therapy using Rituximab induction with maintenance treatment.

The hypothesis is that at least a subset of chronic fatigue syndrome (CFS) patients have an activated immune system involving B-lymphocytes, and that prolonged B-cell depletion may alleviate symptoms.

Professor Geoffrey Burnstock

Professor Geoffrey Burnstock studied theology, maths and physics at King's College London, before completing a PhD at King's and University College London under the supervision of the neurophysiologist, JZ Young. Between 1959 and 1975, Professor Burnstock worked at the University of Melbourne, beginning with a senior lectureship in zoology.

Most of his major research has been on the autonomic nervous system, notably autonomic neurotransmission and he is best known for his discovery that ATP is a transmitter in NANC (non-adrenergic, non-cholinergic) nerves and also for the discovery and definition of P2 purinergic receptors, their signaling pathways and functional relevance.

Professor Burnstock's work in this area has had an impact on the understanding of pain mechanisms, incontinence, embryological development, bone formation and resorption, and on skin, prostate and bladder cancer. Professor Burnstock returned to London in 1975, becoming Head of Department of Anatomy and Developmental Biology at University College London and Convenor of the Centre of Neuroscience. He has served as editor-in-chief of the journals *Autonomic Neuroscience* and *Purinergic Signalling* and has been on the editorial boards of many other journals.

He has been elected to the Australian Academy of Science, the Royal Society and the Academy of Medical Sciences, and was awarded the Royal Society Gold Medal in 2000. He was President of the International Society for Autonomic Neuroscience (ISAN), and was first in the Institute of Scientific Information list of most cited scientists in Pharmacology and Toxicology..

(from The UCL Centre for the History of MEicine)

Continued page 55

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Abstract

Purinergic signalling and CNS disorders

The talk will open with some background information about purinergic signalling, including: its discovery in the early 1970's; the recognition that ATP is a cotransmitter with established neurotransmitters in most nerves in both the peripheral and central nervous systems; the cloning and characterisation of 3 subclasses of receptors for purines and pyrimidines; the widespread distribution of these receptors on non-neuronal cells as well as nerves; and the physiological release of ATP from cells in response to gentle mechanical stimulation and hypoxia. There will then be a description of the distribution of purinoreceptors in the CNS, the importance of purinergic neuron-glia interactions and their roles in normal behaviour. In the last part, studies of the roles of purinergic signalling in CNS disorders, including stroke, ischaemia, neurodegenerative diseases, epilepsy, cognitive, mood and neuropsychiatric disorders will be described and potential novel therapeutic strategies discussed.

Dr. Judy Mikovits

Dr Judy Mikovits is Research Director at the Whittemore Peterson Institute for Neuro-Immune Diseases and has co-authored over 40 peer reviewed publications that address fundamental issues of viral pathogenesis, hematopoiesis and cytokine biology. Formally trained as a cell biologist, molecular biologist and virologist, Dr. Mikovits has studied the immune response to retroviruses and herpes viruses including HIV, SIV, HTLV1, HERV, HHV6 and HHV8 with a special emphasis on virus host cell interactions in cells of the hematopoietic system including hematopoietic stem cells (HSC). Dr Mikovits is one of the authors of the ground-breaking study published in Science magazine in October 2009 which detected XMRV in CFS patients (Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome) and is a member of the US Department of Health and Human Services Blood Working Group.

Researchers at the University of Nevada Medical School have also become collaborators on projects that are vital to our understanding of the immune deficits seen in these patients.

Abstract

Clinical implications of XMRV and MLV-Related (MRV) Human Gamma Retrovirus infection.

In 2009, using a classical virology approach of viral isolation and transmission, electron microscopy, serology and PCR, Lombardi et. al. demonstrated the first isolation of a Human Gamma retrovirus (HGRV): XMRV from blood from patients with chronic fatigue syndrome (CFS) predominately from the west coast of the United States.

In 2010, Lo et al. extended these studies by detecting nucleic acids of MLV-related variants in the peripheral blood mononuclear cells of CFS from the northeastern United States suggesting additional strains capable of infecting humans exist. We have identified several footprints of HGRV infection that can also be used both as therapeutic targets and to monitor clinical trials of therapeutics.

These footprints include clonal TCR gamma rearrangements, B cell populations having a mature CD20+, CD23+ phenotype, which have been shown by our lab and others to harbor XMRV proviral DNA and produce infectious HGRVs. Therefore, XMRV infection may accelerate the development of B cell malignancies by either indirect chronic stimulation of the immune system and/or by direct

Continued page 56

PRESENTERS at the 6th INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

infection of the B-cell lineage. Since viral load in peripheral blood is low, these data suggest that B cells in tissues such as spleen and lymph nodes could be an *in vivo* reservoir for XMRV. In addition, we have identified an inflammatory cytokine and chemokine signature that distinguishes XMRV infected CFS patients from healthy controls with 94% sensitivity and specificity; an XMRV patient population with aberrant methylation profiles consistent with a gammaretroviral infection and a XMRV infected patient population with high nagalase activity. This particular population of XMRV infected patients has responded favorably to treatment with the immune modulator GcMAF. Additional populations of XMRV infected CFS patients have responded favorably to antiretroviral therapy and another population has responded favorably to the immune modulator Ampligen™. Monitoring XMRV viral load, co-infecting pathogens and immune dysfunction affords the opportunity to begin to understand the clinical implications of XMRV/HGRV infection.

Dr. Wilfried Bieger

Dr. Wilfried Bieger is a docent of Medicine in private practice at Applied Immunology Clinic in Munich, Germany. Dr Bieger has been performing a study in co-operation with researchers from Heidelberg University to test German ME patients for XMRV.

Abstract

I will present the results of cooperative efforts undertaken together with Prof. M. Kramer and Prof. R. Wallich from University of Heidelberg in detecting XMRV in German CFS patients. The patients were recruited from all over Germany with a majority in Bavaria. So far, we tested about 80 patients fulfilling all Fukuda criteria for CFS, starting in November 2010 after about 8 months of work to set up a highly sensitive, specific and uncontaminated assay protocol for virus detection in blood. Major advice throughout the experimental period came from J Mikovits who was extremely helpful with methodical advice and testing of parallel samples including sequencing of XMRV specific viral DNA sections. We have also set up a western blot technique for XMRV antibody testing. Blood was taken at my clinic in München and sent directly by mail to the laboratory. We used both heparin and EDTA-blood in the first time but switched over to EDTA alone, which gave better, i.e. more positive results. We could not find viral DNA or RNA in fresh samples except one, but had to cultivate the PBMC for up to 6 weeks under stimulating conditions and partly during coculture with virus permissive LnCap cells. After 2 weeks of culture cells began to turn positive in some patients and continued to display virus for the next weeks. The presence of XMRV was confirmed by sequencing XMRV specific DNA. Recently we started with the antibody tests as well using freshly drawn or deep frozen serum. So far we found retrovirus/XMRV-specific reactions only in a minor proportion of our CFS patients but improvement of the testing procedure is underway.

In conclusion we have no doubt that XMRV is present in German CFS patients although the prevalence may not be as high as reported before in the USA.

Professor Malcolm Hooper – Conference Chairman

Chair of the 6th Invest in ME International ME/CFS Conference 2010 will be Professor Malcolm Hooper, Emeritus Professor of Medicinal Chemistry, University of Sunderland. Professor Hooper is an internationally-renowned expert on ME/CFS and a tireless campaigner for patients' rights. Professor Hooper has previously chaired Invest in ME conferences and participates in The Hooper Interviews - interviews with conference speakers at the Invest in ME Conferences and available on the conference DVDs.



6th Invest in ME International ME/CFS 20th May 2011 Conference Agenda



Start	Presenter	Presentation
07.45	<i>Registration</i>	
08.55	Invest in ME	Welcome to the Conference
09:00	Mrs Annette Whittemore	Key Note Speech: Translating ME/CFS Research into Treatments
09:20	Dr. David Bell	25 Year Follow-up of ME Patients
10:05	Dr. Andreas Kogelnik	Translational Research in ME/CFS
10.50	<i>Break</i>	
11:10	Dr John Chia	Clinical & Research Experience of Enteroviral Involvement in ME/CFS
11:50	Professor Geoffrey Burnstock	Purinergic Signalling and CNS disorders
12:15	Dr James Baraniuk	Cerebrospinal Biomarkers for ME/CFS
13.00	<i>Lunch</i>	
13:50	Professor Tom Wileman Professor Simon Carding	UK Research: Genome Sequencing, Virology & Immunology for ME/CFS
14:15	Dr Øystein Fluge / Professor Olav Mella	B-cell Depletion Therapy Using Rituximab in ME/CFS
15:00	Professor Kenny de Meirleir	Clinical Diagnosis, Treatments and Trials of ME/CFS
15.45	<i>Coffee/tea Break</i>	
16:05	Dr. Judy Mikovits	Clinical Implications of XMRV Research for ME/CFS
16:50	Dr. Wilfried Bieger	XMRV Results from Germany
16:55	Plenary Session	with Professor Malcolm Hooper and BMJ
17.30	<i>Adjourn</i>	



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ME AWARENESS MONTH 2011

People who suffer from Myalgic Encephalomyelitis (ME) are forced to live in a bubble – a bubble created from ignorance



- ME is a neurological illness
- ME patients are banned from giving blood for life
- Over 60 outbreaks of ME have been recorded worldwide since 1934
- ME is 3 times more prevalent than HIV/AIDS - twice as prevalent as MS
- 25% of ME patients are severely affected - housebound, bedbound
- 25,000 patients are children
- ME is the largest cause of long term sickness absence from school for pupils and staff
- ME patients have no approved drugs for treatment
- ME patients have no access to specialist ME consultants
- ME does not discriminate, anyone can be affected
- There is no centre of excellence in the UK that treats and researches ME as a physical illness. UK Charity Invest in ME wants to change that - Please Help Us

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