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The  
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*Mainstreaming*  
ME Research  
*IIMEC8 Conference 2013*

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The Invest in ME conference DVDs are professionally filmed and authored DVD sets consisting of four discs in Dolby stereo and available in PAL (European) or NTSC (N. America) format. They contain all of the presentations from Invest in ME International ME/CFS Conferences (2006 – 2013). Also included in the DVD sets are interviews with ME presenters, news stories and round-table discussions. The Invest in ME conference DVDs have been distributed to more than 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://bit.ly/10YB6n3> or via emailing Invest in ME at [info@investinme.org](mailto:info@investinme.org)



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### 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.

### **Welcome to IIMEC8**

This is our ninth Journal of liME and is made available online for free on the charity's web site. A hard copy also forms part of each delegate's conference pack at the 8<sup>th</sup> Invest in ME International ME Conference 2013.

Invest in ME have now organised eight biomedical research conferences for ME – myalgic encephalomyelitis - and the conference has become a good checkpoint to determine how things are progressing with research into ME.

We have been reminded in recent times of how fragile life is and how healthcare is so important for a just society. Yet for ME services to magically attain the levels for existing diseases, whilst absolutely justified and to be expected, is realistically not something which will appear overnight. Even "established" diseases which have comparatively large research funding and correct perception amongst health departments are not without issues. We have seen examples of this close up.

The key to making ME a disease which receives the highest priority is an objective which we need to attain by establishing basic building blocks and a foundation on which to progress – funding for proper, quality research; education about the disease; and correct perception of the disease. Invest in ME was set up with the objectives of making a change in how ME is perceived and treated in the media, by health departments and by healthcare professionals. These aforementioned building blocks happen to be the basic objectives of Invest in ME.

The people who run and support the charity are all volunteers. There are no salaried staff and all work is performed in spare time, for free. The charity does not exist just to exist – we exist to *make progress*.

For us biomedical research into ME has not been well served in UK or elsewhere for a generation. Patients are literally sick of the behavioural approach to ME and fatigued by the constant false belief that exercise will make one better. The PACE Trial provided evidence that CBT and GET do not produce any objective positive results. Yet although heavily criticised and eventually dismissed by ME patients, with hindsight, perhaps the PACE Trial actually did the cause of biomedical research into ME a huge favour. As knowledgeable patients have been able to point out the flaws in its design, execution and implementation, and debunked implausible attempts to spin the results into a justifiable end point, so the PACE Trial has clearly shown why the psychosocial view of ME is now

seen by mostly all objective observers to be a waste of funding and of lives.

On a more positive and deliberate note the Let's Do It For ME campaign has forced biomedical research into ME - by amazingly positive efforts by people who are not interested in complaining all the time without offering anything - but instead put their thoughts and energy into imaginative ways of crowd funding biomedical research - often pushing themselves beyond their limits.

liME supporters have been showing the real side of ME patients - people wanting to get better and willing to be proactive in achieving this. And thus, by their example, things change.

The promise of treatments developed from the exciting research at Haukeland University Hospital in Bergen has generated campaigns by three European ME Alliance members - Norway's ME Association, Sweden's RMEand Switzerland's Verein ME/CFS to fund this research. The MEandYOU campaign in Norway has an ambitious target to raise 7 million Norwegian Kroner in 90 days and has achieved a commendable result already.

Education is another key to progress. This applies to education of medical professionals as well as politicians, the media, patients and the public. The liME conferences have formed a crucial part of this education and served to provide a platform for the latest and the best biomedical research into ME – demonstrating how false is the belief that little is known about the disease.

The charity has recently completed the distribution of 25 GP packs to GPs and GP clinics in Scotland. The packs contain information about ME, diagnostic guidelines, charity Journal and DVD and other items of specific information about ME which will help the healthcare professional better understand the disease and what progress is being made.

Our conference DVDs allow a historical record of the conference events while at the same time making it available to those around the world who wish to hear of the biomedical research. The charity has heard many times of the usefulness of the DVDs and in many cases where they have helped patients and healthcare staff.

Recently the charity began distribution of the latest ME guidelines – the International Consensus Criteria. Every conference delegate will have a copy in their conference pack. We have also been UK distributor for the printed copies of the Canadian Consensus Criteria.

The charity tries to help people with ME and has been involved in a great deal of campaigning and lobbying to raise awareness and gain a more valid perception in the media and healthcare departments and by the public.

The charity recently met with Dr Martin McShane – NHS Commissioning Board Authority, Director - Domain 2- Improving the quality of life for people with Long Term Conditions). This meeting was requested by the Prime Minister after a constituent and supporter, Alex Hall, met with the PM and passed on a letter from the charity.

At the meeting Dr McShane heard directly from two parents of a severely affected young adult with ME. The parents spoke with dignity and passion about the treatment of their daughter and Dr McShane patiently heard the terrible story of how parents were blamed for this disease affecting their child, and how healthcare services had failed in their daughter's case.

Although not unique such direct imparting of knowledge to a prominent healthcare official of how severely affected patients with ME are managed and treated in UK is relatively rare in our experience.

liME also had proposals to Dr McShane which could be used to move things on.

We suggested using this area (ME) as an example of a difficult area of medicine and use it as a model for nationwide services.

We suggested an ME consultancy role for CCGs to be established.

We proposed setting up clinical trials which could be initiated under the auspices of the local university's clinical trials team. As the NHS can participate and perform research so we suggested two such trials to begin with.

liME proposed setting up a trial of telemedicine, where severely affected patients could be treated by an ME consultant who would not have to be physically present, and where a GP or other professional could sit in and learn about ME.

liME suggested that a standard service model could be used for ME, and tested, in East Anglia. Other commissioning groups would be able to see the

effectiveness and efficacy of this model and it could be developed from there. This service model would be based on a biomedical approach to ME with a trained and knowledgeable consultant(s) and where training was emphasised. GPs could also learn from this and all would be aware of the biomedical research into ME which had been and was taking place. Common protocols could become established to enable a consistent approach to treating patients.

The proposal for an examination and research facility in Norwich by liME includes patients being correctly diagnosed and put forward for biomedical research, with results from the research being applied to patients as soon as possible.

We needed an acceptance from the NHS that there was no one size fits all treatment/management option.

Education of GPs was important as lack of knowledge permeates the NHS. So liME proposed holding workshops with qualified physicians and the charity offered to arrange these as part of the introduction and trial of an appropriate service model, with the charity using its links to various researchers and clinicians here and abroad. Such workshops could educate healthcare staff and look at patients.

We suggested these projects could serve as pilot projects for the NHS commissioning groups.

Dr McShane identified three strands coming from our discussions.

1. Empathy and Respect (anger felt by patients and carers understandable)
2. Services (some in the country supportive)
3. Research

The parents of the severely ill child added a 4<sup>th</sup> important strand - Medical practitioners are faced with a lot of conditions - instead of suspicion they should accept their limitations and show respect. Patient /carer experiences/expertise should be acknowledged.

The outcomes from this meeting confirmed our views that we need to educate GPs; that research is correct way forward as liME were proposing; and that we must continue to have to force through the necessary changes ourselves.

Modern day terms for raising awareness and funding – crowd sourcing and crowd funding – are now used to describe efforts to maximise the potential of new technology for the benefit of patients.

An increasingly more knowledgeable and determined patient population are forcing change and making things happen - making a difference - thanks to conferences and organisations highlighting ME research and to the immediacy and effects of social media.



So an independent charity and its supporters continue to crowd fund biomedical research, continue to crowd source ideas for ME research and continue to raise awareness of this disease – backed by an increasing number of supporters who, themselves, have ideas and are willing to make the enormous effort to make a difference.

Prior to the conference the charity has organised an international collaborative meeting with researchers and clinicians from nine countries in attendance. Last year the collaborative two-day Clinical Autoimmunity Working Group (CAWG) meeting organised by Invest in ME and the Alison Hunter Memorial Foundation of Australia, in London, brought old and new researchers to the same table for two days of discussions.

Initiatives came from this meeting and, perhaps, influenced the latest calls for research in the latest MRC highlight notice from last year -

*“There is now preliminary evidence supporting the view that inflammatory mechanisms in the brain and spinal cord may underlie the pathophysiology of some severe disease CFS/ME phenotypes.”*

*Immune dysregulation: “There is evidence for a disturbance in innate and adaptive immunity in CFS/ME including alterations in cytokine profile, absolute and functional alterations in T cells and NK cells and occurrence of autoantibodies and allergic reactions that may explain some of the manifestations such as fatigue and flu-like symptoms. A number of infectious and*

*environmental exposures have been associated as triggering these changes."*

- UK Medical Research Council

This developing recognition of the real disease in ME needs to be backed up with an appropriate response.

The overwhelming need is for research - and essentially biomedical research into ME. We believe International collaboration is a necessity for research into ME.

If we are seriously to have a way forward for proper research into ME then we need not just adequate funding, but correctly defined cohorts, standardisation on diagnostic criteria and a collaborative of researchers who will not blur science with politics.

Research into ME needs a strategic approach - but it may be destined to fail completely by attempting to establish the way forward on foundations which include so much of what has been wrong in the past. So we need -

- to establish homogeneous research cohorts
- to adopt and endorse the latest ICC or CCC criteria for ME - for research and for diagnosis
- to separate research into fatigue and chronic fatigue from ME
- to establish transparent peer reviewing by professionals with the relevant experience and background

For liME our objectives over the next couple of years will be to attempt to fund more biomedical research using diagnostic criteria that are as good as we have in the current day.

We will attempt to improve education of healthcare staff by facilitating training events with knowledgeable and experienced ME clinicians providing help, advice and education to GPs, nurses, researchers and patients.

We will organise research meetings to bring the best researchers together.

We will collaborate with those who are genuinely interested in progress in researching and treating and curing ME.

We will support those initiatives which promise to make real progress.

Our approach is to try to get a strategic research programme started here in the UK and build collaborations with trusted clinicians and researchers so that patients can get tested as part of research rather than having to spend vast amounts of money travelling to see doctors abroad.

We need clinical trials to get evidence for treatments that work.

We need better education about ME for healthcare staff.

We need additional and long-term funding for biomedical research into ME.

At our IIMEC8 conference we focus on ME now becoming a mainstream research area. We have representatives from most of the main biomedical research initiatives now occurring throughout the world.

Our foundation biomedical research project will begin this year at a leading UK university. We are actively in discussion with a number of other projects and welcome the chance to work with other groups interested in biomedical research into ME.

#### **SPONSORS**

A word of thanks to the Irish ME Trust who, yet again, will be sponsoring one of the speakers to the conference. IMET have been a constant friend and supporter of liME, and of ME patients. They have funded major research into ME and have been a leading member in the European ME Alliance.



This year we would also like to thank the Edward P. Evans Foundation for contributing to the costs of the conference. The Foundation is also a major funder of ME research with recent awards to OMI Merit and Griffith University showing a

commitment and vision which is to be welcomed as we try to facilitate international collaboration and sharing.

And we would like thank our EMEA colleagues in Sweden. RME have kindly donated to help with the costs of the conference.

We would like to thank Simmaron Research Foundation for generously sponsoring the tickets of two medical students from University of East Anglia.

We would like to thank the presenters for coming to London to speak at IIMEC8 and all the delegates who attend in order to make this happen.

We thank all of our supporters for their support in raising ME awareness, for their efforts in funding biomedical research and for their inspiration.

The theme of the 8th Invest in ME International ME Conference 2013 in London on 31st May is Mainstreaming ME Research - an acceptance that, despite the past, research into ME is now joining the mainstream research area deserving of more funding and of the interest of top biomedical research institutions.

The IIMEC8 conference will highlight the major biomedical research initiatives into ME now taking place.

Enjoy the Journal.  
Enjoy the conference.  
Let's do it for ME.

### *Invest in ME*

## **ME QUOTES**

*"The delayed responses starting from 2–7 months after Rituximab treatment, in spite of rapid B-cell depletion, suggests that CFS is an autoimmune disease and may be consistent with the gradual elimination of autoantibodies preceding clinical responses. The present findings will impact future research efforts in CFS."*

*Mella and Fluge, Haukeland University Hospital, Bergen, Norway*

<http://bit.ly/10krfqn>

As part of the conference events this year Invest in ME have organised another researchers meeting in



London.

The Biomedical Research into ME Collaborative (BRMEC) Meeting London on 30<sup>th</sup> May has attending almost 40 of the world's experts and leading clinicians involved with ME.

This meeting follows on from the cooperation and dedication of the Alison Hunter Memorial Foundation (Australia) and Invest in ME (UK).

To raise awareness of ME, and promote collaboration, innovation and foundations for a clearer strategy of biomedical research into ME, Invest in ME and the Alison Hunter Memorial Foundation of Australia continue the collaboration which has been a feature for several years, and which established the Clinical Autoimmunity Working Group which met in London in May 2012.

The extraordinary skill and experience which can be harnessed by meetings such as last year's Clinical Autoimmunity Working Group meeting in London and this year's BRMEC meeting, as well as the possibilities to progress further the understanding of the disease by "crowd sourcing" experience and ideas, promises to enable a unique contribution to understanding ME and suggest future research directions and perhaps treatments.

Chairing the meeting was Dr Ian Gibson, former Dean of Biology at UEA and Professor Hugh Perry of Southampton University and Chair of the Medical Research Council Neurosciences Board.

The objectives of the meeting were:

1. To present the status of some of the latest initiatives occurring in biomedical research into ME

2. To discuss and explore the possibilities for collaboration and for funding for biomedical research into ME
3. To generate new ideas regarding research into ME and assess research strategies for ME research
4. Review experiences and expertise from other research areas in order to assist ME research
5. Review evidence for immunological derangement in ME
6. To discuss opportunities for extending clinical trials in multiple centres and possibly internationally
7. To plan future events

Our hope for the meeting was to initiate new collaborations and generate new ideas for biomedical research into ME and help researchers support each other in the future.

To achieve continued progress in understanding and treating this disease we must establish collaborations between biomedical researchers who can agree a clear strategy of biomedical research.

This demonstrates our view that forming a collaborative of biomedical researchers, including existing ME researchers and those new to the field, is the best way forward and promises the quickest and most efficient way to produce data and treatments and so benefit people with ME and their families – a **Biomedical Research into ME Collaborative** .

Representatives from nine countries attended.

Invest in ME and Alison Hunter Memorial Foundation continue to work together to raise awareness and promote sound biomedical research into ME through collaboration and innovation.

The provisional agenda for the meeting is shown below.

## **BRMEC & IIMEC8 London 2013**

| <b>BRMEC AGENDA</b>   |   |
|---|---|
|  |  |
| Welcome and introductions   |   |
| Pathogen Discovery and Pathogenesis   |   |
| Retroviruses and ME   |   |
| Pathogen Discovery continued  |   |
| Gut Microbiota Study UEA  |   |
| <i>Chaired Discussion</i>   |   |
| Review of experience of Rituximab in ME   |   |
| Rituximab in autoimmune diseases  |   |
| Update on immunological derangement in ME   |   |
| Screening NK-, B- and T-cell phenotype and function in patients suffering from ME   |   |
| <i>Chaired Discussion</i>   |   |
| Update on ANS studies   |   |
| FDA Endpoints / Vistide   |   |
| OMI MERIT Strategy  |   |
| Discussion – As per objectives of meeting   |   |
| Funding Possibilities   |   |
| Ways to Continue Collaboration and Discovery  |   |
| Closing Summary and future directions.  |   |
| Briefing to Invest in ME Conference   |   |

### **ME QUOTES**

*"ME/CFS is not uncommon in England and represents a significant burden to patients and society. The number of people with chronic fatigue who do not meet specific criteria for ME/CFS is higher still. Both groups have high levels of need for service provision, including health and social care. We suggest combining the use of both the CDC-1994 and Canadian criteria for ascertainment of ME/CFS cases, alongside careful clinical phenotyping of study participants. This combination if used systematically will enable international comparisons, minimization of bias, and the identification and investigation of distinct sub-groups of patients with possibly distinct aetiologies and pathophysiologies, standing a better chance of translation into effective specific treatments."*

*Nacul et al. [BMC Med.](#) 2011 Jul 28;9:91. doi: 10.1186/1741-7015-9-91.*



# IIME PROPOSAL FOR RESEARCH and EXAMINATION FACILITY

At the IIMEC8 conference Dr Ian Gibson will announce news of the foundation research for ME project which the charity and its supporters will fund. It is a biomedical research project and will be carried out at the University of East Anglia.

This follows three years of work by the charity and its supporters. It was at the 5th Invest in ME International ME Conference in London in May 2010 that 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 that conference and we decided to publicise our attempt to set up such a facility.

We attached the research to a proposal for a centre of excellence for ME – something which the UK does not have today and which is required. Such a centre would allow proper examinations of people with ME, would allow patients to be put forward for trials, would allow the severely effected to be included in research, would facilitate translational biomedical research into ME to allow early results to be used for the benefit of patients, and would enable a database of results to be maintained.

It may seem straightforward to get research carried out, to organise the necessary elements to treat patients properly, to initiate fundraising to carry this out. In practice it has not been so straightforward.

During this time we have had setbacks. There have been walls put up, some understandable but others mendacious. We have encountered apathy and ignorance from some and lack of support from some.

We have been affected by the effects of the government reforms to healthcare which affected everything in the NHS.

Despite setbacks we have continued to try to get these necessary building blocks for a UK Centre of Excellence off the ground. Invest in ME are a small charity – Small charity BIG Cause has been our slogan.

But we are determined and we have continued to lobby and to arrange and attend meetings. Our

fundraising efforts have continued and the inspiration given by the efforts of supporters has energised us to do more, and never give up.

It does feel that we have been working on this project every single day – and that is close to the truth.

A plain fact of life is that healthcare departments and organisations do not prioritise treatment of ME patients and the recent government healthcare reforms have seriously affected the timescale for implementing this – with a lot of preparatory work lost. The charity has had to spend much time trying to educate people about this disease.

Though there have been a few surprises and disappointments along the way, thanks to wonderful support and help from fellow campaigners, we have managed to get there.

Our work in attempting to set up a clinic, which is linked to the research, continues.

IIME supporters can be truly proud of the fact that a top UK research university is preparing to perform high quality research into ME using sequencing facilities which already exist in Norwich Research Park.

The foundation project looks very good. And so we build on this and continue.

We have other ideas to supplement this and initiate new research. We will continue to try to have proper services for people with ME.

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

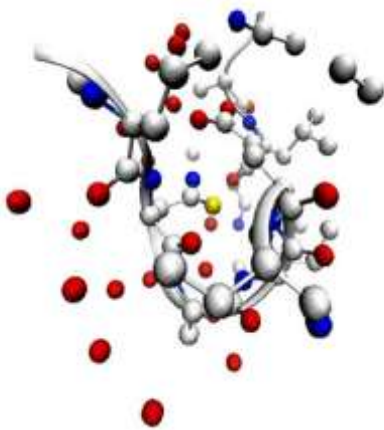
It has taken a great deal of work and determination to pursue this proposal.

But we hope this convinces anyone considering supporting our efforts that we are serious and will continue until we have a proper research base which can make a major contribution to understanding and treating this disease.

## THE CHARITY PROPOSAL-THE BIG CAUSE

With the objective of improving and promoting education about ME amongst healthcare staff and raising awareness of the disease the charity feels that the best way to make progress is to establish a national centre of excellence for ME.

To this end we have established momentum and resources to begin work on establishing a base of research which could develop into a facility leading to a UK Centre of Excellence for Biomedical Research into ME.



## 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 biomedical research being applied and possible treatments not being made available to patients or healthcare staff.

Simplistic and ineffectual, even damaging psychological therapies are offered in place of real treatments - wasting public money and doing nothing to help patients.

This has resulted in ME patients having no real healthcare service and far too little progress in attracting new researchers or clinicians to study the disease. The dangers for people with ME 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 USA Food & Drugs Agency (FDA) recently decided to re-categorise ME in "Immune Diseases -

describing it as "SERIOUS or LIFE THREATENING", on a par with cancer or /heart failure (click here) and the UK government recognise ME as a chronic neurological illness.

To download our poster please use this url - <http://www.investinme.org/Documents/ME%20Awareness/LBM%20Oct2012/Gut%20PROD%20A4.pdf>

## THE AIMS and OBJECTIVES

After five years of campaigning for awareness and promoting better education about ME 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 was formed - consisting of carers of people with ME and scientific advisors - to begin work on establishing a facility leading to a UK Centre of Excellence for Biomedical Research into ME.

We 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 is treated in the UK and establish a hub of scientific and clinical excellence for ME within Europe.

## THE RESEARCH

With the help of leading researchers the charity is proposing a number of initial projects which would help establish a research base and lead to further projects being initiated based on findings.

It is not often realised that 60-70% of the immune system is located in the gut as a vast network of lymph tissue referred to as GALT (gut associated lymphatic tissue). The research highlighted in the proposal involves looking at gut microbiota, which is the latest thinking in how to go about research. In USA, renowned pathogen hunter Dr. Ian Lipkin and specialist clinician Dr. Nancy Klimas have all been suggesting a similar approach.

The charity is keen to replicate the recent Norwegian Haukeland University findings using Rituximab as well as a number of new ideas being developed. The aim is to build on this but the research has to start somewhere and so the researchers will begin afresh with the best approach. This research proposal would build a strategy of research which would involve patients, clinicians and researchers working together.

## THE PROPOSAL

The charity proposes for a facility to be instigated with four main elements for diagnosis, treatment and research into ME – 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.

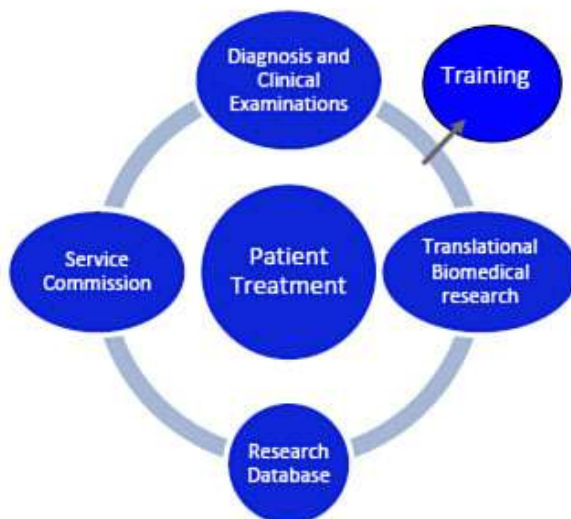


Figure 1

### Service Commissioning

Service commissioning would be performed by the local CCG or CCG Grouping (formerly the PCT). The service would require early and correct diagnosis, examination and treatment of ME 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 would be commissioned by the CCG. 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 or International Consensus Criteria), 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 patients whilst at the same time building up the research database for ME and allowing fostering of new areas of cooperation with other biomedical research facilities.

The research being proposed by 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.

Our initial proposal for research which has been discussed with researchers at the UEA, would aim to initiate studies using TGAC sequencing facility at the Norwich Research Park which would allow all known and unknown 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

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

- Early and correct diagnosis of ME

- the clinical lead consultant would assess and plan the development of future services in conjunction with commissioning CCGs
- 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

- eventual provision of an ambulatory service and/or tele-medical services for those severely ill patients who cannot be moved
- 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
- allow ME 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 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.
- Healthcare staff would feel more comfortable with the diagnosis of ME 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 examination in one area.

The benefits of this approach will, we are sure, save lives and could help restore or improve the lives of hundreds of thousands of patients and their families.

### TRAINING of HEALTHCARE STAFF

The need for training in ME 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 including data on treatments and prognosis.

Specialist advice for more complex cases across the country could be provided based on referrals from

other CCGs. 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.

Our aim is to build sustainable and developing collaborations with translational biomedical research at the heart of all research.



### liME BIOMEDICAL RESEARCH FUND

Our long term 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. We hope to continue raising funds for other

projects and until external research grants are available. <http://bit.ly/qkjD5K>

### HOW TO LEARN MORE

Contact Invest in ME at [info@investinme.org](mailto:info@investinme.org).

### SUPPORT US

Help us by contributing to the Invest in ME Biomedical Research Fund for ME – <http://tinyurl.com/ydh6whu>

Our JustGiving page is here - <http://www.justgiving.com/investinme>



### FURTHER READING

- **University of East Anglia**  
<http://www.foh.uea.ac.uk>
- **Institute of Food Research** <http://www.ifr.ac.uk>
- **Norwich Research Park**  
<http://www.nrp.org.uk/cms.php?pageid=1>
- **Norfolk and Norwich University Hospital**  
<http://www.nnuh.nhs.uk>
- **TGAC - The Genome Analysis Centre**  
<http://www.tgac.bbsrc.ac.uk>
- **EDP News Story**  
<http://www.investinme.org/Medianewspapers.htm>
- **MP Executive Summary September 2011**  
<http://www.investinme.org/Documents/Biomedical%20Research%20Facility/MP%20Exec%20Summary%20September%202011.pdf>
- **FAQ September 2011**  
<http://bit.ly/180lod0>



Let's do it  
for ME!  
*Idifme.org*

Few who have any knowledge or experience of myalgic encephalomyelitis, whether from a personal or professional perspective, would dispute the urgent need for reliable bookmarkers for early and accurate diagnosis and provision of effective medical treatments for this organic chronic disease.

Accurate information, guidance, education and training for patients, public, medical professionals, and other service providers, needs to be made available meanwhile to avoid unnecessary suffering. The Let's do it for ME campaign was launched by a small group of people with severe ME in July 2011 in support of the proposal by Invest in ME to establish a centre of excellence for ME based in East Anglia and the first of its kind in UK/Europe. We commend the forward-planning and joined up thinking to combine translational biomedical research with patient care and education and training for medical professionals, in collaboration with international researchers and like-minded ME organisations across the world, and the clear focus on infection and immunity.

We are keen to help progress research and treatment, not only to benefit ourselves as patients, but also to avoid losing another generation to the ravages of this disease.

We have no more time to lose.

We wished to assist in a practical way by raising the £100k needed to fund the foundation project to get the research strategy underway in Norwich. We were delighted to receive supportive comments for our Guest book or by other means, from some of our MPs; the Countess of Mar, Chair of the Forward ME group; and Jane Colby, Executive Director of The Young ME Sufferers Trust. Empowerment is a key element driving the campaign and it has been very rewarding to see children and young people in particular, as well as the very severely affected, able to play a role in speaking out about their disabling illness and how it is viewed and treated by society and the medical profession,

whilst taking such positive steps to raise funds for the translational biomedical research required to bring realistic hope for their recovery, with support of well friends and family members.

As we expect to reach the initial fund-raising target by the end of May or thereabouts, we will have raised £100k in under two years. This is no mean feat, starting from scratch from our homes and beds, with no campaign budget or publicity. Every penny raised goes to the IIME Biomedical Research Fund; any competition prizes or similar resources are donated.

**Every penny raised goes  
to the IIME Biomedical  
Research Fund**

We could not have achieved this without the tremendous efforts of a wide range of supporters, from very severely ill survivors to wonderful willing wellies.

We are genuinely delighted and appreciative of any types and all levels of support, and there have been too many ingenious, innovative, creative, generous, courageous and inspiring ideas, events and contributions to highlight them all individually.

Our supporters hail from all corners of the UK, Europe, USA, Australia, NZ, and over 3500 votes in April won IIME 1<sup>st</sup> prize of £2000 in The Big Break contest run by Direct Debit.

Writer Jacqueline Rayner is a founder member of our planning group. She had been planning with her friends and colleagues at Big Finish Productions to produce a charity audio play for download in aid of IIME, based on the character of Bernice Summerfield: Many Happy Returns.

Not content with that, producer Scott ran the Edinburgh Marathon for IIME, Simon donated funds

from his choir, and others have done more besides. At the same time, planning group member and writer Barnaby Eaton-Jones reworked his play, *Running To Stand Still*, in aid of our cause.

Music artist Mama Chill decided to proactively support IIME in her awareness raising and by donating proceeds of downloads and joining the team. Her ME Awareness track is based on the original "I Can't Stand The Rain", and her new track, "Don't Say Nuthin If It Ain't Worthwhile" was released for May Awareness. There are various other artists, writers, musicians, photographers, supporting IIME.

Members of the planning group run the campaign websites and on-line shops; organise May Awareness events such as The Big Sleep for ME, designed to be accessible to people of all ages and levels of illness severity and launched in 2012, ongoing fundraisers such as the 1<sup>st</sup> of each month One Day-One Pound and Small Change to Change M.E, the Christmas card competition, calendars and summer quizzes, card sales, stalls, supermarket and church collections.

We also proactively support other patient initiatives that include IIME such The Big Shave 2013 and Walk for ME. This is all done painstakingly between us over the course of days, weeks, months.

Make ME Crafts exploded onto the scene last year and is proving hugely popular, with an ever-expanding team producing an impressive range of arts and crafts available all year round.

A young contributor summed it up with this comment:

"Big thankyou to Jon because you have brought the community together, its really positive, everyone is happy making and doing things they enjoy and its all going to hopefully find what is going on with our bodies !! Sooo happy to be a part of this XD xx"

Another member of our planning group featured alongside an advert placed by IIME to raise awareness of the foundation research project. Rosa had previously crocheted soft wool blue awareness wristbands for IIME and her grandparents hosted a coffee morning in aid of our cause.

Following a decline in her health, Rosa was moved to a nursing home, and fed by nasojejun tube. She chose to mark her 21<sup>st</sup> birthday by raising awareness and funds for our cause. The staff at the nursing home joined in with a pyjama day with all proceeds to Rosa's appeal.

Goodwill messages were posted across the social networking sites and some people used Rosa's photo as their profile picture for the day.

Her mother said that the appeal passed all their expectations. Having contracted ME at 8 years of age, Rosa's story epitomises the indomitable spirit of the majority of people of all ages with ME, as well as the spirit of our campaign.

A 14 year old boy wrote:

"Although it has been a year since I was in hospital due to M.E. I am still struggling with this awful misunderstood illness. I am still not in school and I want my life back as I knew it. I know many other children who are suffering with this illness too and I am in touch with them. They are also missing out on so many things like me. This is such a great cause, raising money to find a cure!!"

We are grateful to IIME and to all those who are engaging with the international drive to instigate, fund, and conduct the kind of high quality scientific biomedical research that may be translated into long-awaited effective treatment options for this organic disease.



Wherever you are based and whatever role you play, be it front of stage or behind the scenes: we thank you for your support.

Here follows just a few of the campaigns set up by supporters to raise awareness of ME and to raise funds for the liME Biomedical Research Fund.

**Big Finish Productions** is pleased to announce a very special release to celebrate the twentieth anniversary of archaeologist and adventurer Bernice Summerfield.

**Many Happy Returns** will be a unique feature-length drama where every penny will go to supporting Invest in ME.



**Stacy Hart** aka Rap/Hip Hop artist **Mama Chill** is an ME sufferer with real talent. When diagnosed with ME doctors told her that any chance of a music career was well and truly over but Stacy didn't let this discourage her. While bed-bound for two years she released 13 track home demo rap/hiphop album 'RAW' and also entered and won a competition to write a song for Victoria



Beckham on Channel 4's Richard and Judy. This positive feedback encouraged her back into the studio where she worked with producer Shane Shanahan on her next album 'Nobody wants to know ya when ya Nobody'.

**The Big Sleep for ME** is an awareness and fundraising event initiated by Julia Cottam as part of the Let's do it for ME effort to raise awareness and funds for biomedical research.



**One Day One Pound** encourages donations of £1 to be made on the 1st each month. If you would like to join us in creating a sea change by donating just £1 (or more if you wish) one day a month for Biomedical ME Research text the code ODOP99 £1 to 70070.





**Make ME Crafts** is a creative branch of the Let's do it for ME campaign initiated and run by ME sufferer Jon Watson which sells handmade and unique items made by ME sufferers and their supporters crafting for charity.



**'Running To Stand Still'** is a charitable audio play with original songs. The central theme is the illness ME and, aside from giving information about the disease, it revolves around how it affects relationships and a sufferer's life. It is in aid of Invest in ME and all the professional creatives involved have graciously given their time for free for this production.



**Advertisement**

*"If I'd had this book when I first became ill, things would be very different"*

**Nancy Blake**  
B.A., CQSW, UKCP Accredited Neurolinguistic Psychotherapist. Became ill with ME in 1986, now virtually recovered.

**Leslie O. Simpson**  
Ph.D. Hemorheologist with years of research into the impact of non-deformable erythrocytes on the symptoms of ME.

'A Beginner's Guide to ME/CFS' is an emergency manual for people who are just discovering that they have ME. You need to know that you are not your illness, that ME is a serious physical disorder, and that you must rest, for quite a while, at the beginning, and continue to limit exertion. Adding Les Simpson's recommendations to a regime of rest, right from the beginning offers a further means of improving your well-being. These two measures can create the possibility of gradual improvement over the long term.

'Ramsay's Disease' is comprehensive account of the history of ME, and the history of Les Simpson's involvement with ME research, conferences, and patient groups. It also provides a detailed account of the science behind his recommendations. And much more of Nancy's story.

Both books recommend radical changes to current medical practices and public policy.

Order from Amazon and all good bookshops. Kindle e-book editions also available.

# Lili – Diane's Story

## *An ME Carer's View*

I'm a carer for my adult daughter, Lili, who is completely bedbound with very severe myalgic encephalomyelitis. For Lili, M.E. didn't come slowly. It very rudely crashed into her life and very quickly stole her health, taking bigger and bigger chunks of it as she deteriorated.

It all began when she experienced a gastric virus of a sort she had never experienced before because this time she never regained her health. A couple days later, she woke up with agonising head pain 'like her brain was on fire', with severe neck pain – she also couldn't move her neck, and her whole body was paralysed. She's not sure how long she stayed like this as she was in and out of consciousness but she truly felt that she was going to die because her body was undergoing an extreme crisis.

To cut a long story short, it took a year to get a diagnosis during which time she literally dragged herself to doctors and hospital appointments to undergo tests and consultations (which were sometimes more like inquisitions from paid torturers).

Although Lili was severely affected and completely housebound from day one, she forced herself to go because she so desperately wanted to know what was wrong with her so that she could have treatment and get on with her life again. However each visit and test pushed her body beyond its limits.

She was gradually deteriorating.

Every tiniest activity (physical, cognitive and sensory) from washing her hair to rubbish collection day, had devastating results.

Sometimes she could recover in a few days, other times it would take months, but often the cumulative effects of the noisy, smelly, bright, sunny, loud, vibrational, fast, chemical based world we live in were all too much and disease progression with permanent damage resulted. Doctors always amaze me when they are puzzled by her severity and wonder why it's taking so long to 'pick up her bed and walk'.

Lili collapsed after her last hospital visit. She passed out with a seizure, her body violently shook, and paralysis spread throughout her body. It was an extreme reaction to the overload of physical, cognitive and sensory attack on her body during that year, but this last journey to the hospital was the straw upon the last straw that broke her body down.

She never recovered.

My beautiful daughter is totally bedbound. She has a diversity of symptoms that seem endless. (Most of the very severely affected have between 60+ and 100+ symptoms). The worst thing of all is the relentless, agonising pain. Widespread pain in every muscle, joint, and organ possible.

She has not had one day free from pain since the illness began.

Her whole life now is lived from her bed. Not her choice for she is a talented artist and photographer and she dreams of being in summer meadows photographing the dancing bees and butterflies and painting the colourful flowers.

She dreams of baking cupcakes. She dreams of completing her geology degree. She dreams of paddling in the sea with her nephew. She dreams of putting on a pretty dress with her hair all beautified. Such simple dreams.

Her dreams have been snatched from her by this awful disease that others misunderstand by thinking it's just about feeling tired or attention-seeking.

The above are some of Lili's dreams but in reality, she would just love to be able to do some of the everyday things that others take for granted. Lili longs for simple pleasures such as having a bath, cleaning her own teeth, reading a book, eating a plate of solid food, emailing her friends, cuddling her nephew, having a conversation, going to the toilet rather than using a slipper-pan, and having a hug.

When I hear people moaning about having to stand in a queue, I think 'my daughter would love to do that' (not the moaning bit)! To be able to get up, have a shower, get dressed, walk, travel, shop, interact with the environment, have a conversation, and stand in a queue are such blessings that people

forget they have. And to be able to do all this without unimaginable pain is a further blessing.

My amazing daughter has such a positive view of life. I'm stunned that she's not depressed or angry. Although she sometimes has her low days, her courage and inner strength are immeasurable. Not a day passes without seeing one of her magical smiles which sometimes just breaks my heart.

Her days are spent in a darkened room and in as much silence as the outside environment will allow. She is hypersensitive to light, noise, odour, vibration, touch, movement, chemicals, some foodstuffs, and medicinal drugs. She can hear a vacuum cleaner five houses down the road, smell the fabric softener on people's clothes and feel the vibration of a humming fridge. All these things can send her body into a crash at any time.

She is unable to sit or stand due to being moribund with pain, orthostatic intolerance, paralysis, blackouts and much more and so her bed is her companion twenty-four hours a day. She is unable to chew and has swallowing difficulties so her food is liquid or puréed. She cannot tolerate touch as her skin is always 'on fire' like it's been grated with a cheese grater. Her description. I have to cut her pyjama tops off (when she can tolerate a change of tops) because any movement causes her indescribable pain. She has difficulty speaking sometimes and so asks me to be her voice...

***"My amazing daughter has such a positive view of life. I'm stunned that she's not depressed or angry. Although she sometimes has her low days, her courage and inner strength are immeasurable. Not a day passes without seeing one of her magical smiles which sometimes just breaks my heart."***

I do my best to protect her from noise, light, odour, vibration, movement etc within the house to minimise the damage to her health. I pick up the pieces after a visitor has long gone, desperately trying to create a place of healing safety for recovery to occur and to reduce her recovery time. However, I

am limited to protecting her from the outside world - aircraft, motorbikes, fireworks, DIY, sunshine, heat, barking dogs, roadworks, lawnmowers, parties, environmental smells...the list is endless. Another thing that I try to protect her from is people's attitudes towards her illness and therefore, towards her personally. Sometimes these misunderstandings and judgemental opinions come knocking at your door.

Last year we had to move house. There was no choice. Lili and I knew that it would be a huge cost to her health and in the back of our minds, we knew (but didn't verbalise), it could have taken her life too. It didn't but it came very close. With a move comes new doctors. I registered us both at the local surgery straight away and booked a home visit. I won't go into details but the GP was an aggressive rude man who insulted Lili to such a degree that I wanted to throw him out. I remained polite but firm. The next time I called the surgery I requested a different GP. She came as if she had already prejudged us. The doctor was very keen for Lili to do GET. Lili declined stating her reasons.

A couple of months later there was a knock at the door. It was a social worker. One of the doctors (who wished to remain anonymous) made an allegation of abuse/neglect. I was in a state of shock and felt sick to my stomach. To hear the words 'suspected of abusing your daughter' is something that will haunt me for the rest of my days. The accusing doctor said that Lili was 'being kept in the dark', 'not allowed to speak', 'nursed in bed for 24hrs for 3 years', 'denied hospital appointments'. The film, 'Whatever happened to Baby Jane?' springs to mind doesn't it! The case is still ongoing.

Lili and I were hurled out of our safe world into the jaws of ignorance and betrayal. The bond of trust between patient and doctor had been shattered. It was obvious that the accusing doctor had no basic understanding of M.E. (let alone very severe M.E.). No understanding of light sensitivity and the fact that this group of patients are unable to get out of bed and so they certainly cannot travel to hospital appointments. The extent of this ignorance in a doctor is just frightening. The fact that they have not kept up their medical knowledge is cause for grave concern.

The carer of an M.E. loved one is like no other carer. Not only is it imperative to learn about myalgic encephalomyelitis in order to give the specialist care required for M.E. (to avoid causing them further

harm), it is also necessary to become their protector. This serious illness is very misunderstood, even by doctors. Society as a whole has a very misguided view of M.E. and so the carer has to do all they can to keep this harmful ignorant tribal thinking from entering the world of the M.E. sufferer. They need to protect their healing space from influences, opinions and 'treatment' that will cause disease progression and maybe even death.

But who protects the carer? In some ways the carer is as vulnerable as their loved one. If a doctor does not respect a patient's choice of treatment, they can send in the heavy mob – social services. It's not just children with M.E. that this happens to but adults too. Adults, like Sophia Mirza, who are completely of sound mind are threatened or taken away from the safety of their home and family. Another way to force the seriously ill person to tow-the-line is to go after their carer. A doctor can say anything they want. They are believed because of their social standing. People with M.E. don't seem to have the right to choose their treatment like other seriously ill people do.

This can be a lonely and difficult journey for the M.E. person and their carer to travel. Together they travel, often feeling alone, often feeling vulnerable, feeling ignored and misunderstood, feeling isolated from a world they once knew. But this world no longer recognises them, no longer understands their plight, their sorrows, their torment, their daily struggle. They are outcasts.

**“Doctors and healthcare workers need to be re-educated, and the media and general public need correct and truthful information. People need to know... because M.E. isn't fussy who it attacks next.”**

My hopes and prayers are that things will change for the better for the M.E. community and their carers. New M.E. biomedical centres with specialist training for healthcare workers would be a good start. I wholeheartedly support Invest in ME and their campaign to create a centre of excellence which is much needed not only for those with myalgic encephalomyelitis, but for society as a whole. Doctors and healthcare workers need to be re-

educated, and the media and general public need correct and truthful information. People need to know... because M.E. isn't fussy who it attacks next.

## ME QUOTES

*Ann Epidemiol. 2013 Jun;23(6):371-376. doi: 10.1016/j.annepidem.2013.04.003.*

*The adoption of chronic fatigue syndrome/myalgic encephalomyelitis case definitions to assess prevalence: a systematic review.*

*Johnston S, Brenu EW, Staines DR, Marshall-Gradisnik S. Griffith Health Institute, School of Medical Sciences, National Centre for Neuroimmunology and Emerging Diseases, Griffith University, Parklands, QLD, Australia.*

*CONCLUSIONS: Advances in clinical case definitions during the past 10 years such as the Canadian Consensus Criteria have received little attention in prevalence research. Future assessments of prevalence should consider adopting more recent developments, such as the newly available International Consensus Criteria. This move could improve the surveillance of more specific cases found within CFS.*

<http://www.ncbi.nlm.nih.gov/pubmed/23683713>

## ME QUOTES

*"It is of the greatest importance to keep in mind the goal toward which one works in science, but it is also of equal importance to simply explore and define the 'new' while keeping that mind well prepared for finding new treasures. It is only through such efforts that we believe the etiology of CFS will be finally illuminated."*

*Steven Tracy and Nora Chapman, University of Nebraska Medical Center:*

<http://bit.ly/11Xs9MA>

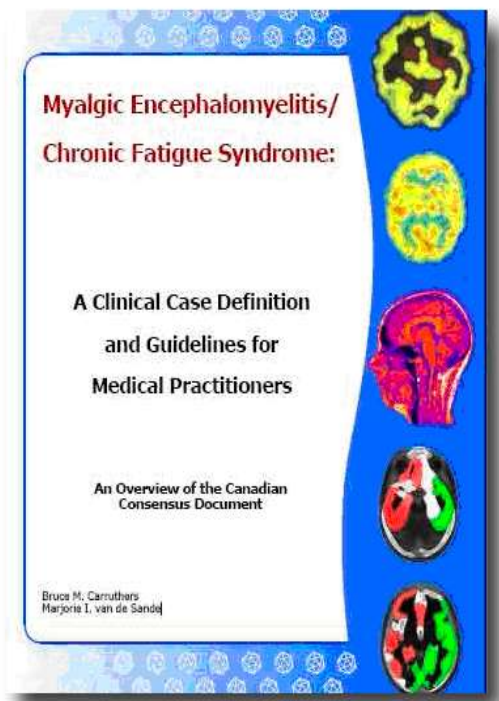
# GUIDELINES

One of the basic problems with treatment of ME is the original diagnosis of the illness. Invariably it is too late and the current environment in the UK means that diagnosis may cover a broad range of illnesses with similar symptoms which are brought together under one diagnosis - ME - a dead-end of a medical diagnosis by a medical community which cannot even agree on a name.

In order to establish correct and early diagnosis there needs to be a standard clinical diagnosis method used throughout the country. This area is currently clouded with up to four sets of diagnostic criteria being available for use.

When a doctor or paediatrician gives a diagnosis of myalgic encephalomyelitis then they do this currently by exclusion of other illnesses and by means of basic blood tests.

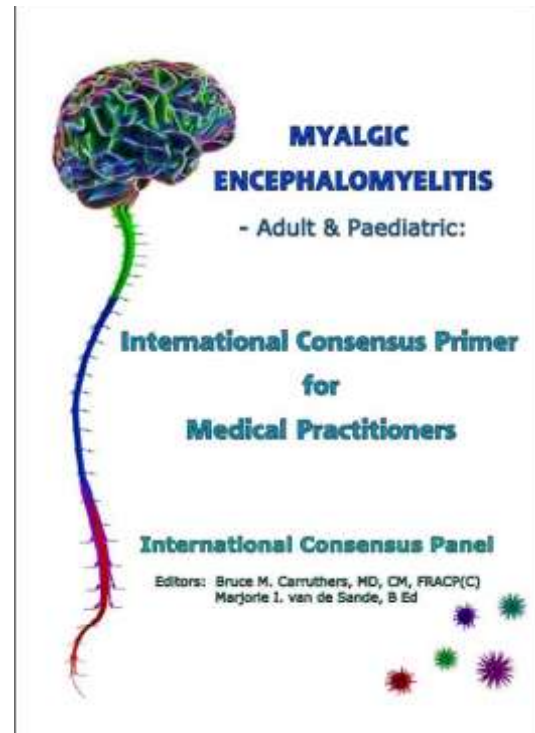
Diagnostic guidelines are meant to be a means to assist in diagnosis. Another important distinction is



between guidelines used for research and those used for clinical diagnosis.

One may think these would always be the same. A clinician may treat a wide selection of patients but researchers need cohorts that are as homogeneous as possible.

If a diagnosis is given to a patient based on a different interpretation of an illness then the diagnosis may be flawed. Worse still patients might be misdiagnosed and a treatable illness may be missed for years in some cases. Invest in ME support the use of either the so called Canadian Consensus Criteria (CCC) or the later



version of these guidelines the International Consensus Criteria (ICC).

For some time Invest in ME have been responsible for distributing printed copies of the Canadian Consensus Guidelines in the UK.

The charity earns nothing from this – we merely attempt to recover the cost of the original printing.

The Canadian guidelines were recently endorsed by the US CFS Advisory Committee.

More recently the International Consensus Guidelines (ICC) has been produced and is available in printed form from Invest in ME.

Contact [info@investinme.org](mailto:info@investinme.org) to order.

# Helping IiME – Sarah's Story

Invest in ME's supporters have achieved an enormous amount over the years. One of the continually impressive ways of raising awareness of ME and of achieving fund raising to support biomedical research has involved use of our JustGiving pages.

Continuing in the ethos of IiME and the methods of Let's Do It for ME - to make progress and not build egos and to try to enjoy, as best one can, the events and ideas generated to support the charity – this nevertheless often masks some of the real tragedy being endured and the sacrifices people have had to make.

So we have picked out just one story. Sarah-Louise Jordan is raising money for IiME and biomedical research.

## My Story

There is so much I want to say!

Before I became ill I hadn't even heard of M.E and the first twelve years of my life were magical and very English.

Then I had a vaccination against meningitis c and my health very quickly began to fall apart. At first it was just all kinds of aches and pains, dizziness, forgetfulness, nausea, the occasional fainting spell and a lot more tiredness but within two years I had a constant migraine and I struggled to drag my legs around because they were so heavy.

Soon I couldn't walk at all and I began to 'freefall' until I was blind and had no memories. I lost all of my words and my ability to understand other people speaking. I was so exhausted even when I woke first thing that it felt like I was trying to lift buildings to try and move.

I was housebound for a year and I by the end of it I could stand for 30 seconds and manage a few painful steps, but then I relapsed again and became bedbound. I didn't sit up for four months, I barely moved and I couldn't talk. I had no sense of touch and no strength in my body. I suddenly perked up in April 2004 and could sit up and read a little, I was so

excited. In July 2004 I woke up to find my whole body 'on fire'. So hot it felt like I was melting, so painful I wanted to scream and scream and scream. I honestly didn't think I could bear it for one minute. So far I have been on fire for eight and a half years and counting....

At first the pain, the heat and the pressure-which made my head feel like it was gripped in a vice- was so intense that I couldn't move or speak again. For six and a half years I was silent and still, simply enduring, my hearing was so sensitive that I had to wear headphones all the time.

My parents added another door to my room and triple glazed the window. every noise was still excruciating. I had blackout blinds because the light made me physically sick. I released a strange chemical that smelt acidic and clung in clumps to my hair, pooling in white/brown patches on my skin.

I woke one day to find my hands curled in fists, rigid, paralysed and I couldn't open them.

Nothing seemed to change until 2010 when they opened enough for me to be able to use my 'claws' and I began to be able to do little things despite the fire, like read and write and go online.

I am still bedbound, although I had a little time when I could move around the house last year, and the fire has been particularly awful again this last year.

I am 25 years old and I so want to live.

I could write books worth on everything that has happened, but really all I need to say is, Invest in M.E are actually doing something to help people like me...and there are hundreds of thousands of us.

We all fight the same dragon; we all want to beat it so we can be free.

And I can't even tell you how heroic my M.E friends are, what they go through and also how kind they are to other people! If you don't know them, you are missing out!

With them and the girls from my old schools, and other people I've met along the way, I feel that I have a life rich in people. But I am a young, free

spirit trapped in a body that will not work! Invest in ME want to change that.

And, as to losing the 50 lb, it is something I really need to do, although I do not know who is going to keep Mr. Kipling in business without my help ;)

### Sarah's JustGiving Page

Sarah's fundraising page is here -  
<http://www.justgiving.com/Sarah-Louise-Jordan>

Thanks for taking the time to visit my JustGiving page.

M.E is a horrible illness suffered by over 250,000 people in the UK and no cure or cause is currently known. I'm raising money for research into M.E as it's an illness that I and many of my close friends suffer from and I want to do my bit to help change that!

I've taken the following information off the charity's website because I think it explains things better than I can:

*'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 biomedical research being applied and possible treatments not being made available to patients or healthcare staff.*

*Simplistic and ineffectual psychological therapies are offered in place of real treatments - wasting public money and doing nothing to help patients.*

*This has resulted in ME patients having no real healthcare service and far too little progress in attracting new researchers or clinicians to study the disease.*

*The dangers for people with ME 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.'*

Donating through JustGiving is simple, fast and totally secure. Your details are safe with JustGiving – they'll never sell them on or send unwanted emails.

Once you donate, they'll send your money directly to the charity. So it's the most efficient way to donate – saving time and cutting costs for the charity.

So please dig deep and donate now.

Invest in ME's JustGiving pages are here -  
<http://www.justgiving.com/investinme>

## JustGiving™

Companies can also use JustGiving to support Invest in ME. The more awareness and funds we can raise the sooner there will be treatments for people such as Sarah.

### ME QUOTES

*"ME/CFS is disabling and has a greater impact on functional status and well being than other chronic diseases such as cancer. The emotional burden of ME/CFS is felt by lay carers as well as by people with ME/CFS. We suggest the use of generic instruments such as SF-36, in combination of other objective outcome measurements, to describe patients and assess treatments."*

Nacul et al. BMC Public Health 2011, 11:402

<http://www.biomedcentral.com/1471-2458/11/402>

### ME QUOTES

*"After acute infections, enteroviruses can persist in patients resulting in manifestation of ME/CFS. Chronic enterovirus infection in an immunocompetent host may be an example of a stalemate between attenuated, intracellular viruses and an ineffective immune response." , Chia, Chia: EvMed Research, California, USA*

<http://bit.ly/10krfqm>

# PRESENTERS at the 8<sup>th</sup> INVEST in ME INTERNATIONAL ME CONFERENCE

## Bios and Abstracts from the presenters at IIMEC8

### Conference Chair - Dr Ian Gibson



Former Dean of Biological Sciences, UEA

Dr Ian Gibson, former Labour MP for Norwich North, worked at University of East Anglia for 32 years, became Dean of the school of biological sciences in 1991 and was head of a cancer research team and set up the Francesca Gunn Leukaemia Laboratory at UEA. In 2011 Dr Gibson received an honorary doctorate of civil law from UEA.

### Key Note Speech: The Mainstreaming of ME Research

#### Dr Daniel Peterson – Simmaron Research Foundation



With over 25 years of medical practice, Dr Daniel L. Peterson has become a sought-after internist for diagnosing difficult and complex medical cases. When several patients in Incline Village became ill with symptoms that resembled persistent mononucleosis, Daniel Peterson was one of the first physicians to

recognize an outbreak of what is known as ME/Chronic Fatigue Syndrome (ME/CFS). He became a pioneering physician and researcher in understanding the biological characteristics and methods for diagnosing, managing and treating ME/CFS. He has also performed major studies of Ampligen as a treatment for ME/CFS, and studying the possible role of human herpes virus 6 (HHV-6) in CFS patients. See Wikipedia entry - click here [http://en.wikipedia.org/wiki/Daniel\\_Peterson\\_\(physician\)](http://en.wikipedia.org/wiki/Daniel_Peterson_(physician))

### Key Note Speech: Making ME Mainstream: Strategies for ME Research and Collaboration

#### Dr Andreas Kogelnik

Director of the Open Medicine Institute, USA



Dr Andreas 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. 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.

Abstract: Not available at time of printing – but will be available on Invest in ME web site.

## The Role of the Brain and ME

### Rakib Rayhan



Rakib Rayhan works with Dr James Baraniuk at Georgetown University, Washington, and is deeply interested in symptomatic development and chronification of pain and fatigue in idiopathic illnesses such as Myalgic Encephalomyelitis (ME),

Gulf War Illness (GWI), and Fibromyalgia (FM). Understanding pain perception, autonomic and cognitive dysfunction in relation to abnormal functional and structural changes within the brain in GWI has been Mr. Rayhan's specific focus for the 2 past years.

He has discovered that white matter alterations in the right inferior-frontal occipital fasciculus are strongly associated with the severity and perception of pain and fatigue. In addition, he has identified two unique phenotypes based upon autonomic and hyperalgesic changes in response to an exercise-challenge.

Changes in symptoms were associated with distinct patterns in working memory cognitive networks and discrete regions of brain atrophy. These recent discoveries have substantiated GWI as a central nervous system disorder. He is actively engaged in further pursuing a systems biology approach to the neuroimaging research by examining genomics, proteomics and metabolomics.

His desire is to identify potential biomarkers that provide objective support to disease criteria and that are then translated into new and affordable therapies leading to a better quality of life for patients.

### Abstract

Myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a disabling and complex disease state characterized by profound fatigue, chronic pain, autonomic dysregulation, headaches, sleep disturbances, cognitive dysfunction, endocrine, immune and exertional exhaustion. ME/CFS is a part of a larger group of idiopathic interoceptive and nociceptive illnesses such as Gulf War Illness (GWI), Irritable bowel syndrome (IBS), migraines and Fibromyalgia (FM). Such syndromes greatly impair quality of life and have a high economic burden. Despite considerable research ME/CFS, GWI, and FM are diagnoses of exclusion that is further complicated by symptom severity, subphenotypes and a lack of quantifiable objective biomarkers.

Exercise based paradigms have been useful models to show dynamic symptom alterations in CFS/ME and FM. This raised the question of whether increased susceptibility to stressor paradigms can elucidate objective evidence for the entire symptom complex. Utilizing both exercise provocation and functional magnetic resonance imaging (fMRI) technology, Dr. James Baraniuk has developed a novel paradigm to characterize the causality between inappropriate stressor response and

neurological dysfunction in GWI. GWI affects 25-30% of the one million military personnel who served in the 1991 Persian Gulf War. Veterans with GWI present with multifaceted symptom profiles similar to ME/CFS patients. In fact, overlap in symptoms often leads to co-morbid diagnosis.

The data presented today provides the first direct evidence of i) white matter damage that is associated with the complaints of pain and fatigue ii) elucidation of two phenotypes in response to exercise stressors iii) neurological evidence of compensatory cognitive function iv) cortical, cerebellar, and brainstem damage associated with exercise induced phenotypes and v) cognitive alterations associated with abnormal energetics of lactate metabolism in the prefrontal cortex possibly linked to neuronal mitochondrial dysfunction.

An important confounder is the use of different designation criteria to diagnose patients. This has created difficulties for clinicians to identify cases and also hindered meaningful collaboration between researchers. Current phenomenological case definitions have considerable consistency and functional overlap. What is clear is the need to shift focus from aetiology and "symptoms at rest" to the response of the CNS to physiological perturbations. Although heterogeneity in symptom complexes exists; it may be too subtle to elucidate true subphenotypes at baseline. This is due to the remarkable ability of the brain to recover function and hide the underlying insult. Pushing the CNS beyond its compensatory capabilities removes the phenotype dependent functional stopgap and leads to unchecked pathophysiological profiles that amplify subgroups that would otherwise go unnoticed.

We propose that fMRI of patients before and after stressor protocols may provide the distinct advantage of a standardized top-down approach that will lead to biomarker discovery of subphenotypes, individual pathophysiology, and tailored therapies.

## Retroviruses and ME

### Professor Greg Towers

Professor of Molecular Virology, Research Department of Infection, Div of Infection & Immunity, University College London, UK  
Research Activities: HIV, Host factors influencing viral tropism and antiviral innate immunity, Innate

Immunity, Retrovirus in gene therapy and xenotransplantation, Transcription and chromatin



### Abstract

Greg J Towers and Stephane Hue  
Infection and Immunity, University College London

Why do we think that XMRV is not a human pathogen?

Xenotropic murine leukaemia virus related virus (XMRV) is a mouse gammaretrovirus. In 2006 XMRV was described as being present in prostate cancer samples using a new technique of virus discovery. Several labs began to study the association between XMRV and human disease. In 2009 XMRV was associated with samples from patients with ME/Chronic Fatigue. This study raised particular interest because it also found XMRV in samples from healthy controls suggesting that XMRV may be a new human pathogen infecting millions of individuals.

Our interest in studying the life cycle of retroviruses led us to consider whether XMRV was truly a human pathogen. We found that patient derived XMRV sequences were almost identical to a mouse xenotropic gammaretrovirus found in a human prostate cancer cell line called 22Rv1. Using phylogenetic techniques we could show that the sequences in the cell line were more diverse and parental to those derived from patients. We also found that some XMRV sequences were identical to another known gammaretrovirus called Moloney MLV, a virus that is commonly used to study MLV and that cannot replicate in human cells.

We concluded that XMRV sequences in patients could be explained by contamination, a recognised problem with very sensitive PCR based detection methods.

We went on to show that human integration site junctions described as proving XMRV infection of human prostate samples could also most likely be explained by contamination.

We also demonstrated that MLV sequences detected in patient samples by Shyh-Ching Lo and colleagues did not represent evolution of XMRV, rather

contamination of patient samples with different MLV sequences from mouse genomic DNA.

We were unable to find XMRV sequences ourselves in HIV patients in the UK or within prostate cancer samples in the USA. In 2011 Vinay Pathak and colleagues described how XMRV is a recombinant virus that arose in the procedure in which the 22Rv1 cell line was derived by passage of human tumours in mice. The complex recombinant nature of XMRV and the lack of viral infection of tumour samples before exposure passage in mice convincingly demonstrated that the source of XMRV was contamination of PCR reactions with DNA from 22Rv1 cells or cloned XMRV encoding plasmid. These results and their implications for future retrovirus research in ME will be discussed.

We are funded by the Wellcome Trust, the Medical Research Council and the UCL/UCLH National Institute of Health Research Biomedical Research Centre

## Pathogen Discovery in ME

### Professor Mady Hornig

Associate Professor Mady Hornig, Center for Infection and Immunity (CII), Columbia University Mailman School of Public Health, New York, USA



Mady Hornig, MA, MD is a physician-scientist in the Center for Infection and Immunity (CII) at the Columbia University Mailman School of Public Health where she serves as Director of Translational Research and is an associate professor of epidemiology.

Her research focuses on the role of microbial, immune, and toxic stimuli in the development of

neuropsychiatric conditions, including autism, PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection), mood disorders and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).

She is widely known both for establishing animal models that identify how genes and maturational factors interact with environmental agents to lead to brain disorders and for her work clarifying the role of viruses, intestinal microflora and xenobiotics in autism and other neuropsychiatric illnesses that may be mediated by immune mechanisms.

Under her direction, proteomic analyses of umbilical cord samples are identifying potential birth biomarkers for autism in a prospective study in Norway, the Autism Birth Cohort (ABC).

She established that there was no association between intestinal measles virus transcripts and autism, and, with Brent Williams and W. Ian Lipkin at CII, has found altered expression of genes relating to carbohydrate metabolism and inflammatory pathways and differences in the bacteria harboured in the intestines of children with autism.

She also leads projects examining the influence of immune molecules on brain development and function and their role in the genesis of schizophrenia, major depression, and cardiovascular disease comorbidity in adults, and directs the Chronic Fatigue initiative Pathogen Discovery and Pathogenesis Project at CII.

In 2004, Dr. Hornig presented to the Institute of Medicine Immunization Safety Review Committee and testified twice before congressional subcommittees regarding the role of infections and toxins in autism pathogenesis.

Her work in ME/CFS is establishing immune profiles and helping to identify pathogens that may be linked to disease.

Her work on the MIND (Microbiology and Immunology of Neuropsychiatric Disorders) Project, one of the largest studies of immune factors in mood disorders and schizophrenia, examines the role of viruses and immune responses in the pathogenesis of these disorders.

Abstract: Not available at time of printing – but will be made available on Invest in ME web site.

# NHS Reforms: Implications for long term chronic conditions such as ME – for GPs and Patients



**Dr Clare Gerada** MBE MOM FRCP FRCGP  
Chair, Royal College of General Practitioners

Dr Clare Gerada is a London-based GP and Chair of Council of the Royal College of General Practitioners. She is the first female Chair for over half a century. She has held a number of local and national leadership positions including Senior Medical Adviser to the Department of Health. She is Medical Director of the largest practitioner health programme in the country and she has published a number of academic papers, articles, books and chapters.

Dr Gerada has been a GP since 1992, when she became a partner for the Hurley Clinic in South London. The practice started life in 1969 – and remains on its current site – on the ground floor of a 19-storey housing estate in Lambeth. Dr Gerada has a long involvement with the RCGP; she was previously Vice Chair of College Council and past Chair of the Ethics Committee. She established the RCGP's groundbreaking Substance Misuse Unit and also led on the strategic and logistical delivery of the RCGP Annual National Conference.

Prior to general practice, she worked in psychiatry at the Maudsley Hospital in South London, specialising in substance misuse. She was awarded an MBE for services to medicine and substance misuse. In 2012 Dr Gerada was presented with the National Order of Merit award in Malta for distinguishing herself in the field of health.

## Abstract

Government NHS Reforms: Implications for long term chronic conditions such as ME – for GPs and Patients

The Health and Social Care Act 2012 makes provisions for a number of changes to the English NHS – these changes became operational on 1 April 2013. Dr Clare Gerada, Chair of the Royal College of GPs, will present an overview of the NHS Reforms, and what changes in legislation mean in practice for GPs and their patients.

Her talk will cover the structural changes, accountability, funding arrangements and commissioning. Dr Gerada will also outline the role of the Royal College of GPs, and ongoing work on long-term conditions.

## Current Knowledge of Immunological Biomarkers in ME

### Professor Sonya Marshall-Gradisnik

School of Medical Sciences, Griffith University, Australia



Professor Marshall-Gradisnik is one of Australia's foremost researchers in the area of neuroimmunology and has been instrumental in establishing the

Public Health and Neuroimmunology Unit (PHANU) at Bond University. Much of her work relates specifically to autoimmunity in Chronic Fatigue Syndrome sufferers and she is regularly asked to speak to community groups on behalf of Queensland Health and NSW Health.

Her research in the area of exercise immunology has also contributed to the body of knowledge relating to the effect of doping in sport and she serves as Sports Medicine Australia's national spokesperson in this area.

The vital research conducted by Professor Marshall has attracted more than \$1 million in grant funding and she has produced 21 peer-reviewed papers, five

book chapters and one provisional patent. In 2008 Dr Marshall was joint leader of the Bond University team responsible for developing the BioSMART program. The team was awarded a prestigious Australian Teaching and Learning Council Award (formerly known as the Carrick Award) for Outstanding Contribution to Student Learning and for the quality of student learning over a sustained period of time.

**Abstract:**

Immunological and molecular markers for defining Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis

S.M. Marshall-Gradisnik<sup>1,2\*</sup>, T.K. Huth<sup>1,2</sup>, K. Fuller<sup>1,2</sup>, M. Kapur<sup>1,2</sup>, S. Johnston<sup>1,2</sup>, S.B. Ramos<sup>1,2</sup>, D.R. Staines<sup>2,3</sup> and E.W. Brenu<sup>1,2</sup>

1. School of Medical Science, Griffith University, Gold Coast, Australia

2. The National Centre for Neuroimmunology and Emerging Diseases, Griffith Health Institute, Griffith University, Gold Coast, Australia.

3. Queensland Health, Gold Coast Public Health Unit, Robina, Australia

Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (CFS/ME) is disorder with hallmarks of varying changes in immune cells and molecular related mechanisms. Decreased cytotoxic activity of innate and acquired immune cells together with increased CD4+, CD25+, FOXP3 regulatory T cells (Tregs) are consistent in CFS/ME patients, while cytokine profiles and immune cell phenotypes have produced equivocal results. MicroRNA and B cell investigations have also provided potential insight into additional immunological and genetic markers for CFS/ME.

More recently investigations of NK phenotypes, dendritic cells (DCs), neutrophils, B cells, T cells,  $\gamma\delta$ T cells and Tregs as well as cytotoxic activity, expression of cell surface receptors, adhesion molecules, intracellular proteins and cytokine secretion have been reported for CFS/ME patients.

Collectively these studies are reviewed, suggesting comprehensive dysregulation of the immunological response in CFS/ME suggesting impaired immune functioning characterised by inadequacies in eliminating pathogens and restoring immune tolerance.

## Clinical Immunology and Research on B-cell Abnormalities in ME Patients

### Dr Amolak Bansal



Consultant Clinical Immunology and Immunopathology, Epsom and St. Helier University Hospitals NHS Trust, Surrey, UK

Dr. Bansal trained in immunology and allergy from 1989 to 1993 at St. Mary's Hospital in Manchester and at Hope Hospital in Salford. From here he spent five years (1993-1997) as Senior Lecturer and Consultant in Clinical Immunology in the Department of Medicine at the Princess Alexandra Hospital in Brisbane, Australia. From 1997 to the present date Dr. Bansal has worked as a Consultant in Clinical Immunology and Immunopathology at Epsom and St Helier University Hospital. Dr Bansal's key interests lie in allergy, autoimmunity, CFS/ME and immunodeficiency.

**Abstract:**

**B and T cell dysregulation in patients with CFS/ME**

Bansal AS, Bradley AS, B. Ford B Sutton CFS Service and Department of Immunology, St. Helier University Hospital NHS Trust, Carshalton, Surrey, SM5 1AA.

Low level autoimmunity is frequently evident in patients with CFS. However, CFS patients do not have the clinical features or the repertoire of auto-antibodies seen in the commonly recognised systemic connective disorders or organ specific autoimmunity. Nonetheless, B cell depletion using Ritiximab has shown benefit in CFS. Furthermore

autoimmunity to non-conventional self proteins has also been demonstrated.

We sought evidence for B cell dysregulation as well as T cell dysfunction in 33 well characterised patients with mainly moderate CFS fulfilling all recognised criteria. B, T and NK cell enumeration was assessed using flow cytometry and NK cell cytotoxic function by K562 killing. Cytokines were analysed by multiplex technology.

We found a significantly increased number of naïve and transitional B cells in addition to reduced plasmablasts in patients with CFS compared to healthy controls. The numbers of switched memory B cells were also reduced suggesting a dysregulation of B cell checking mechanism. CFS patients had significantly greater numbers of T helper memory effector cells and T helper and cytotoxic effector cells. They also had significantly reduced numbers of CD8+ lymph node homing naïve and memory T-cells suggesting either sequestration within lymph nodes or a reduction overall. While the levels of proinflammatory cytokines were no different between the CFS patients and the HC, the levels of IL12, IL21 and IL27 were reduced. These cytokines are particularly involved in regulating cellular immunity and specific antibody production within lymph node germinal centres. We did not find any significant difference in the circulating levels of NK cells or in NK cytotoxic function between patients with CFS and the HC.

Taken as a whole our data suggest a subtle impairment of the immune system with T and B cell dysfunction geared towards autoimmunity and reduced anti-viral immunity. This was accompanied by altered lymph node germinal centre formation that is critical for specific antibody formation and the elimination of B cells with autoimmune tendency. We speculate on the cause of these changes in immune function which are likely to be multifactorial.

## Immunological Basis of ME

### Professor Carmen Scheibenbogen

Professor for Immunology and Deputy Chair, Institute of Medical Immunology, Berlin Charité, Germany  
Group leader of a Tumour Immunology Laboratory and Attending Physician at the Dept. of Haematology, Oncology und Transfusionsmedizin,

CBF, Charité,,2/1997 Venia legendi for Internal Medicine "Habilitation",1990 - 1998 Residency at the Med. Klinik und Poliklinik V, Hämatologie, Onkologie und Rheumatologie, Universität Heidelberg, 1988 - 1990 Postdoctoral fellowship at the Med. Klinik, Dept. of Hämatologie und, Onkologie, Universität Freiburg,1982 - 88 Medical school at the Universities of Bonn, Marburg and Denver



### Abstract: Diagnostic Markers in CFS

One of the major problems in CFS is that the diagnosis is based on symptoms reported by patients. Diagnostic tests would be of great benefit for improving diagnostic uncertainty and the performance of clinical trials. A hallmark of CFS is immune dysregulation and immune activation. Both T cell activation and a skewed T cell type 1 / 2 profile can be detected in many patients with CFS. Regarding B cell function both diminished and elevated levels of immunoglobulins are found in subsets of patients. Further a skewed immune response against EBV is frequently found. Thus it should be possible to develop reliable diagnostic tests based on immune abnormalities.

## B-cell Depletion Therapy Using Rituximab in ME/CFS

### Professor Olav Mella

Bergen University Hospital, Norway  
Professor Mella and Dr Fluge have published a paper "Benefit from B-Lymphocyte Depletion Using the Anti-CD20 Antibody Rituximab in Chronic Fatigue



Syndrome. A Double-Blind and Placebo-Controlled Study".

## Dr Øystein Fluge

Bergen University Hospital, 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 Depart. of Molecular Biology, University of Bergen.

### Abstract:

#### **Intervention and maintenance treatment with the B-lymphocyte depleting monoclonal anti-CD20 antibody Rituximab in ME patients. A Phase II study.**

**Fluge Ø, Mella O.** Dept. of Oncology and Medical Physics, Haukeland University Hospital and University of Bergen, Norway.

We have previously published a case series and a small double blind, placebo-controlled study using immune manipulation with the B-lymphocyte depleting, monoclonal anti-CD20 antibody Rituximab (Rtx). These studies showed that Rtx yielded clinically meaningful responses, with symptom alleviation, although usually transiently, in the majority of patients. Patients in the double-blinded study having received placebo were according to protocol offered inclusion into an open-label Phase II with Rtx treatment. This study pursued the concept of repeated Rtx infusions to see if responses were more durable than in the randomized study, and to estimate side effects of the drug including adverse effects of prolonged B-cell depletion.

28 patients (including 2 pilot patients) were treated with Rtx 500 mg/m<sup>2</sup> day 1 and 15 (as in the randomized study) and with maintenance Rtx infusions at 3, 6, 10 and 15 mths. Patients in slow responses were offered additional infusions up to 24 mths. Study endpoints were predefined according to

the criteria defined in the randomized study. The main endpoint defining response was change in Fatigue score during the observation period, although improvements in fatigue were generally followed also by decrease in other ME-symptoms. Follow-up is a minimum of 28 mths in all patients.

Two patients had serious allergic reactions and had to stop Rtx treatment (one responding patient given alternative B-cell depleting agent with new response). Two had repeated airway infections and were given antibiotics and eventually gamma globulin. Seven had transient ME-symptom increase shortly after Rtx infusion. Two had late onset neutropenia of short duration.

20 of the 28 patients had moderate or major response to treatment. 7 of the 9 placebo patients from the randomized study (without response) responded in the present study. Median self-estimated level of functioning, compared to completely healthy condition, was changed from 10% at baseline to 78% at 18-24 mths after inclusion in responders, and from 15 to 18% in non-responders. Response durations were evidently longer than in the randomized study. However, later than 24 mths into the study, 9 of 20 responding patients have had ME-symptom recurrences. We conclude that the present Phase II study supports previous data on good clinical responses to immune manipulation with Rtx in ME-patients and that maintenance treatment seems to prolong responses. Based on the studies, we have sought financial support for a Norwegian multicenter, double-blinded and placebo-controlled study of Rtx given at day 1 and 15, and at 3, 6, 9 and 12 mths, with 24 mths observation time. This study will also include prospective analyses of bio bank material and physical tests to verify the subjective measures that are the prime endpoints.

Parallel to the clinical studies, we have performed multiple analyses to get a better understanding of the mechanisms that trigger and maintain the symptoms in ME. Although preliminary, this has given us a candidate system we presently are investigating as a possible effector system in the body that may explain the symptoms and responses to interventions in ME-patients. What could be a possible link between such a system and the immune manipulation that Rtx induces? Dr. Fluge will cover this aspect of our studies in his presentation at the meeting. Supported by the Kavli Foundation and the Western Norway Health Authority.



# OMI-MERIT INITIATIVE



For a long time IIME has argued for a strategic approach to research into ME was necessary. But a translational research model also requires research to be connected to patient care – diagnosis, management, treatments, research integration, follow-up and so on. In such a model we also need researchers to work together. International collaboration is necessary and sharing of common database repositories and protocols. Local area GPs and consultants need to be involved and be able to share experiences.

The use of digital technology also needs to be integrated in order to expedite and facilitate research and results. Using new technology also opens the way for severely affected patients to be integrated into research – thus enabling opportunities for them to be able to improve if treatments are found.

The OMI-Merit Initiative offers to do all of this and create a surge of awareness which can finally make the urgent and long-overdue leap in progress which has been held back for a generation. Invest in ME wish to play a part in supporting this endeavour. The OMI-MERIT Initiative is a strategic initiative of the Open Medicine Institute and its collaborators to put the best science and people together in an organized, collaborative plan to discover and apply diagnostic and treatment solutions for ME/CFS. Led by the Open Medicine Institute and the MERIT Chair, Dr. Andreas Kogelnik (Open Medicine Institute/Private practice, US), the OMI-MERIT includes already many of the leading clinicians. Leading scientists and clinicians from around the globe with expertise in immunology, virology, genomics, informatics, molecular biology, epidemiology, infectious diseases, oncology, pathology, and clinical medicine – many presenting at IIMEC8 or BRMEC this year including Dan Peterson (Private practice, US), Olav Mella and Øystein Fluge (Haukeland University Hospital, Norway), Sonia Marshall-Gradisnik (Griffith Univ., Australia), Carmen Scheibenbogen (Charité Berlin, Germany), Rosamund Vallings (Private practice, New Zealand) and Mady Horning (Columbia Univ., US).

## The OMI-MERIT Priority Projects

The OMI-MERIT initial projects are as follows –

### **1) Treatment: Phase 1: A large-scale, randomized, placebo-controlled trial of rituximab and valgancyclovir**

*Goal:* This rigorous, four-armed study will examine and further validate two of the most promising

therapies in the field by comparing: placebo, rituximab alone, valgancyclovir alone & combination therapy of valgancyclovir plus rituximab. Exceptional measurements of physiologic, genomic, virologic, and immunologic markers will be made throughout the course of the trial.

*Importance:* A large-scale, rigorous trial is needed to confirm the initial findings of earlier smaller studies and move ME/CFS to molecularly trackable disease. Success of such a trial could move ME/CFS to a mainstream process for additional diagnostic and treatment trials.

### **2) An International Neuro Registry and Biobank- Partially Funded.**

*Goal:* Supporting and expanding the largest and most comprehensive, longitudinal ME/CFS information source for research and collaboration will be the result of this project. We will collect longitudinal data and biological specimens from ME/CFS patients and controls and characterize the ME/CFS population by patient symptoms, laboratory and molecular profiles through crowd-sourced informatics and cutting edge tools in immunology, genomics and molecular biology. Comprehensive, standardized, sampling will include blood, CSF, urine, stool, brain/CNS, and other tissues. Samples will be available for additional studies in the MERIT list and beyond.

*Importance:* There has been no large-scale, chronologic characterization effort across the ME/CFS population. The Registry and Biobank will help establish clinical and biologic clusters in the population, paving the way for diagnostic biomarkers and cluster specific treatments. In addition, this will provide a community resource for patients and is central to additional collaborative projects.

### **3) Protein Panel in Treatment and Naïve Patients**

*Goal:* Performing in-depth, cutting edge protein analysis of selected specimens from the Biobank to identify bacteria, viral, hormonal, antibody, cytokine and other protein-based substances that might be present in patient specimens. Specimens will be selected based on expected yield from clinical data and then discoveries confirmed in the larger patient population.

*Importance:* This project aims to apply cutting-edge protein detection systems with specific, ultra-sensitive ME/CFS related targets identified. Protein markers are key in identifying potential biomarkers and many new advanced technologies have never been applied to ME/CFS before.



#### **4) Treatment: Phase 2: Other therapy mono and combination pilots**

*Goal:* To assess the effect of other touted treatments that are currently available in the field and establish immunologic and molecular parameters for measuring the efficacy of such treatments.

Treatments assayed will include: Ampligen, Famvir, Etanercept, Rifaximin, Issentris, and possibly others.

*Importance:* To determine a direction and baseline for other potential drug therapies in the field and assess which should receive additional allocation of funds for research.

#### **5) Immunologic Biomarker Exploration Studies**

*Goal:* These exploratory studies will examine B-cell, T-cell and Natural Killer cell responses to disease and treatment groups using comprehensive, rigorous methods many of which have never before been applied to ME/CFS. It will seek to establish immunologic baselines and variants from that across the patient population.

*Importance:* For a disease that appears to have a solid immunologic component to it, this study will provide the most advanced, longitudinal characterization of immune changes in critically implicated cells over selected treatment and control patients.

#### **6) DNA Genetics-Funded**

*Goal:* Use the most advanced methods to sequence key areas of the human genome in a set of patients and controls and affected families and unrelated individuals. Utilizing advanced Human Genome Project technologies, this project will undertake HLA and other regional sequencing of areas of interest for selected patients and families.

*Importance:* Establishing or refuting a role for genetics and potential heritable risk in ME/CFS.

#### **7) Mass Spectroscopy/Environmental Measurements**

*Goal:* This exploratory study will search patient samples for unknown compounds, toxins, proteins and other substances that may be implicated in the genesis of the disease or otherwise contribute to immune dysfunction.

*Importance:* This would be the first systematic examination of samples by the most reliable substance identification techniques to begin to establish an understanding of the contribution of nutritional and environmental factors to ME/CFS.

#### **8) Comprehensive Viral Testing**

*Goal:* Establish a core of viral testing methodologies that are useful and could be useful clinically. Testing will include blood, urine, and saliva and other tissues where available for specific viruses such as EBV, HHV6, CMV, Parvovirus, HSV1, HSV2, and additional

panel type testing for novel viral identification and high throughput methods.

*Importance:* This project will set the standard for clinical viral testing in ME/CFS and establish a guideline for evaluation and treatment directions for patients. Priority given to assays that have already yielded promising clinical results in partner labs.

#### **9) Advanced Immunologic Biomarker Study 2**

*Goal:* This secondary immune study will look at additional cell types that complement project #5 above, such as monocytes, macrophages and dendritic cells.

*Importance:* This study extends our immunologic understanding of the disease and its extent.

#### **10) Treatment: Phase 3: Natural and Over-the-Counter substances-Moringa pilot funded**

*Goal:* Examine the potential benefit of several over the counter/natural therapies in a vetted scientific setting. Substances examined will include: Moringa oleifera, GcMAF, Vit B12, and Artemisinin.

*Importance:* This project will be a first application of vetted scientific method and molecular science to non-pharmacologic substances that have had anecdotal benefits reported, thereby setting a standard for mainstream measurement of ME/CFS.

#### **Answers to inquiries:**

1. The studies are listed in priority order, voted on by the OMI-MERIT group, however each study will start as soon as it's funded. We have several donors that have specified which project they will fund. We will announce them as we are funded.

2. We have been fully funded for the OMI-MERIT, Project #6, DNA Genetics study and we have been partially funded for Project #10, a Moringa oleifera study, and partially funded for Project #2 the Registry and Biobank.

3. We will make announcements via Press Release, the OMF e-newsletter, the OMI Website & Facebook

4. The Open Medicine Institute (OMI) is a Community Benefits Corporation committed to applying a multi-disciplinary, big data approach to the health care system to advance the understanding of "difficult" diseases and improve patient outcomes.

5. The Open Medicine Foundation (OMF) is a U.S. 501(c)(3) nonprofit with an aggressive mission: Invest in accelerating collaborative medical research to find effective treatments and diagnostic markers, current focus, ME/CFS.

Keep the community informed by disseminating information on current research projects and results. Bring together thought leaders from around the world to brainstorm and participate in targeted initiatives.

Encourage and engage the patient community to take an active role in their own health care.



# 8<sup>th</sup> Invest in ME International ME Conference 2013 31<sup>st</sup> May 2013, London Conference Agenda



| Start       | Presenter                          | Presentation  |
|-------------|------------------------------------|---|
| 07.45-08.50 | <b>Registration</b>                |   |
| 08.55       | Dr Ian Gibson                      | Welcome to the Conference   |
| 09:05       | Dr Daniel Peterson                 | Key Note Speech: The Mainstreaming of ME Research   |
| 09:20       | Dr Andreas Kogelnik                | Key Note Speech: Making ME Mainstream: Strategies for ME Research and Collaboration               |
| 10:05       | Rakib Rayhan                       | The Role of the Brain and ME  |
| 10:45       | Plenary                            | <i>Questions</i>  |
| 10.50       | <b>Refreshment Break</b>           |   |
| 11:10       | Professor Greg Towers              | Retroviruses and ME   |
| 11:40       | Professor Mady Hornig              | Pathogen Discovery in ME  |
| 12:25       | Plenary                            | <i>Questions</i>  |
| 12.30       | <b>Lunch</b>                       |   |
| 13:20       | Dr Clare Gerada                    | Govt NHS Reforms: Implications for long term chronic conditions such as ME – for GPs and Patients |
| 13:50       | Professor Sonya Marshall-Gradisnik | Current Knowledge of Immunological Biomarkers   |
| 14:35       | Dr Amolak Bansal                   | Clinical Immunology and Research on B-cell Abnormalities in ME Patients                           |
| 15:05       | Plenary                            | <i>Questions</i>  |
| 15.10       | <b>Refreshment Break</b>           |   |
| 15:30       | Professor Carmen Scheibenbogen     | Immunological Basis of ME   |
| 16:10       | Professor Olav Mella               | B-cell Depletion Therapy Using Rituximab in ME/CFS - I  |
| 16:40       | Dr Øystein Fluge                   | B-cell Depletion Therapy Using Rituximab in ME/CFS - II   |
| 17:10       | Plenary                            | Dr Ian Gibson - <i>Questions</i>  |
| 17.30       | <b>Adjourn</b>                     |   |



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**The Open Medicine Institute – Advancing a Collaborative, Multidisciplinary Approach to Health Care and Research  
OMI-MERIT – ME/CFS Strategic Plan.**



The **Open Medicine Institute** is proud to have **Invest in ME** as a partner supporting the advancement of ME/CFS diagnosis and treatment. For information on the OMI-MERIT research project please visit:

<http://openmedicineinstitute.org/research-initiatives/mecfs-merit/>

Get involved and help us build a global registry to drive ME/CFS research with a target of more than 20,000 ME/CFS patients.

Pre-register today at the link below. OpenMedNet will open to the general public this summer.

<https://www.openmednet.org/registration/MECFS>

OpenMedNet is an community building platform developed by OMI that facilitates and promotes collaboration (patient consented and HIPAA compliant) from all sources (patient, caregiver, physician, hospital, lab, researcher and others) for the purpose of collecting data to better understand ME/CFS.

OpenMedNet helps you keep track of your health, while also helping your physicians manage your care and giving you the option to contribute to medical research. All data is maintained securely and confidentially according to your preferences.

# IS THIS WHERE THE CAUSE of ME LIES?



**We'd like to find out!**

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. This is one project UK Charity Invest in ME wishes to initiate to determine whether changes in the gut microbiota contribute to ME. Other biomedical research projects will follow. Please support our proposal for an examination and research facility for ME in the UK and help us to help people with ME. Let's Do It for ME.

See - <http://www.investinme.org/research.htm>

**Invest in ME** (UK charity nr. 1114035)

[www.investinme.org](http://www.investinme.org)

email: [info@investinme.org](mailto:info@investinme.org)

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