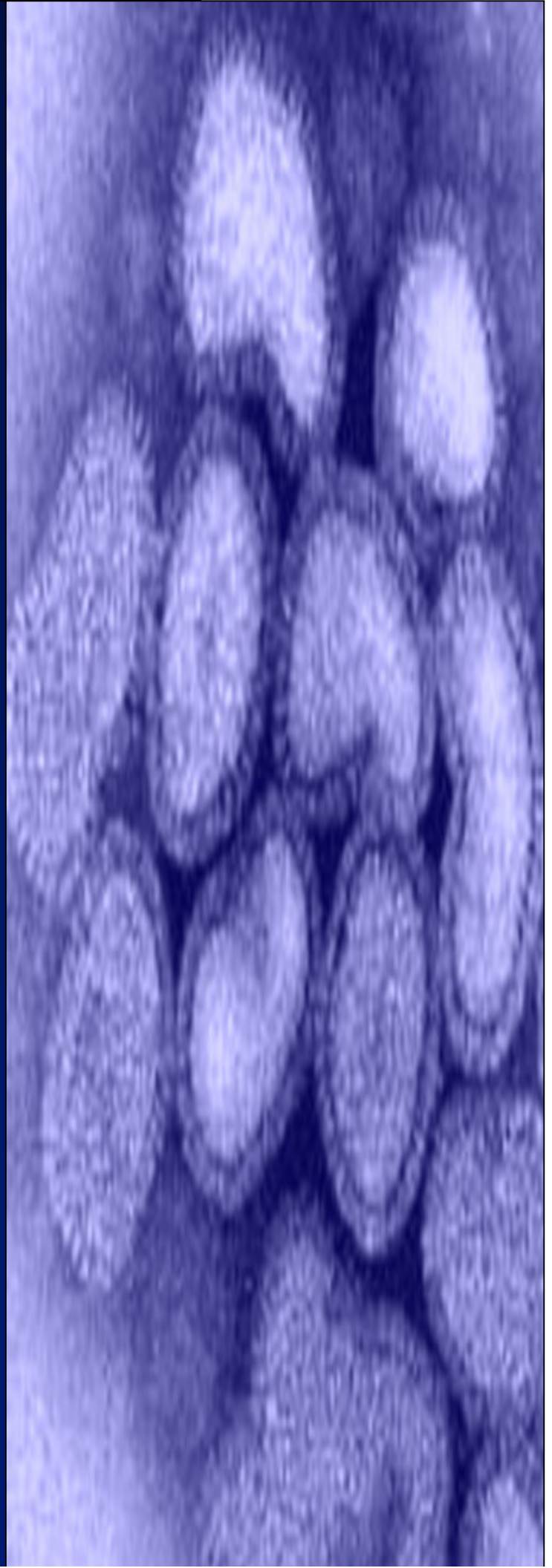


The Journal of IiME

Volume 3 Issue 1

***from
Invest in ME***



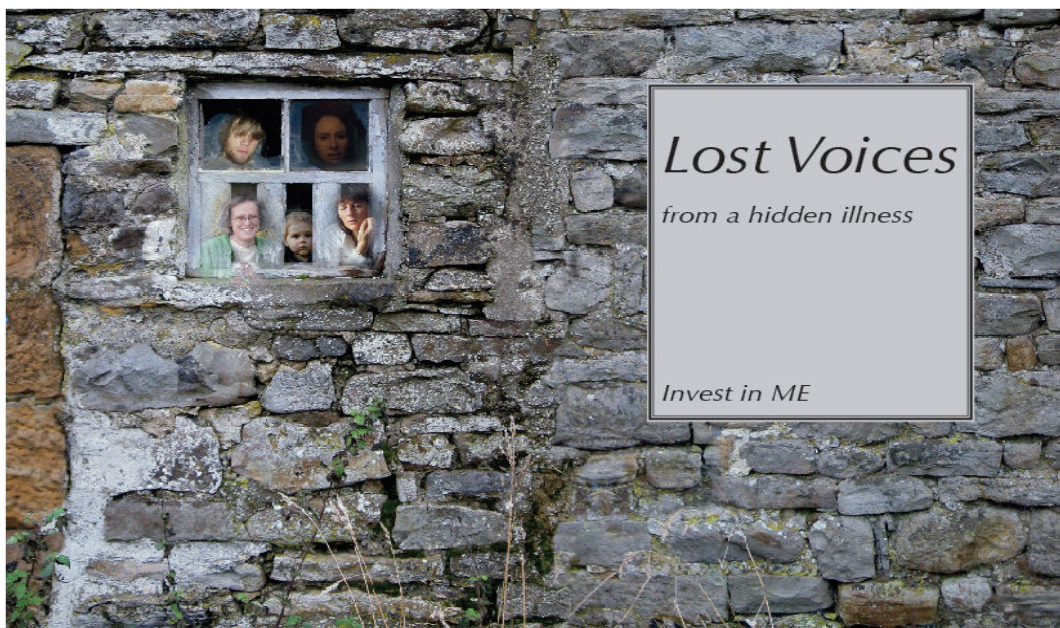
LOST VOICES

Providing a voice for those severely affected with myalgic encephalomyelitis

Invest in ME has published a book which we hope will help healthcare professionals, media, ME Support groups and people with ME in their quest to improve education regarding Myalgic Encephalomyelitis (ME).

The name '**Lost Voices**' refers both to the fact that people who are severely ill with ME are generally not in a position to make themselves heard, and also to the way that the prejudiced denial of ME - as an 'aberrant belief' rather than a devastating physical

- It clearly and movingly shows the evidence of the devastating impact this physical disease has on individuals and their carers and families
- It will bring to more public notice the plight of ME sufferers
- It will help change a widespread lack of comprehension based on general misinformation, vague definitions and manufactured statistics, to the development of empathy and concern for those who are so ill



illness - has meant that often others are incapable of actually hearing and seeing what is being said and shown.

'**Lost Voices**' is primarily written by people affected by severe ME- whether as sufferers, carers or families.

The book provides the following -

- It allows an opportunity for people who are usually invisible and unheard to speak for themselves, so that their situation can be seen and understood more clearly

- It can educate the medical profession, the public and others such as wider family
- It will, hopefully, encourage a sense of community among ME sufferers and those supporting them

The book is an A4 landscape size with a laminated card cover.

The stories and photographs are provided by carers, families and, as far as possible, people with ME themselves. '**Lost Voices**' represents

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different families, showing the impact of the illness on all family members and sufferers and carers.

The book is of extremely high quality and is offered by Invest in ME at a reasonable price to allow more people to be able to purchase it.

With around 120 pages of stories, pictures and information this is without doubt the only book around which truly encapsulates the tragedy of this illness and the way in which people with ME are left to exist in a twilight zone - left to deal with this illness by themselves.



The moving stories convey the real picture of ME.

And yet **Lost Voices** will show the resilient character of people with ME and their families.

The book also contains facts about ME with contributions from experts such as Dr. John Chia, Dr Leonard Jason, Dr Vance Spence and Annette Whittemore of the Whittemore-Peterson Institute.

If there is one book on ME that you buy then make it **Lost Voices**.

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

This book can really make a difference.

To order **Lost Voices** email to info@investinme.org or go to our web page at –

[[http://www.investinme.org/LostVoicesBook/IiME Lost
Voices home.htm](http://www.investinme.org/LostVoicesBook/IiME%20LostVoices%20home.htm)].

Support ME Awareness – Invest in ME

Lost Voices

A view from Oliver, whose older sister has severe ME

"**Lost Voices**" is not just a book about ME/CFS, rather it is a book that has been created and written by the very people who experience the illness first hand; severe sufferers, their carers and their families.

The combination of photographs, images and writing found in **Lost Voices** beautifully express the realities of the illness and its impact not only on the sufferers but on their friends and families as well, giving a voice to so many people who have been left to fight this debilitating illness in isolation.

It does not just tell one person's story or even one family's story. **Lost Voices** brings together and shares the stories of many different individuals, families, carers and friends; each story unique, each story providing an insight into a world that has been invisible to most people for too long.

Anyone who has suffered from or is still fighting ME/CFS will find **Lost Voices** a powerful and uplifting reminder that they are not alone, that there are so many others like them, fighting for recognition, fighting for understanding and fighting for fair and effective treatment. This is a book full of love, courage, hope and determination.

This book is not just for those suffering from ME/CFS but is also for their carers, friends and family members. You can share the experiences of others who have been sucked into this hidden and isolated world. It provides an invaluable way of explaining this illness and its impact to those who are fortunate enough not to have experienced it first hand.

Lost Voices contains contributions offering insight and expertise from leading figures in the ME/CFS research and support community.

The forward has been written by Leonard Jason, former Vice President of IACFS/ME: -

'...Lost Voices will help healthcare professionals and others become less

judgmental, and more tolerant and understanding of those with ME, for these are the voices of heroes...

there were moments of wonder when I realized that these patients have something uniquely profound to share with a world so saturated with materialism...

these patients are asking us to wake up from our stupor...

Their courage and life affirming stories challenge us to act. Just as the Civil Rights and Women's movements focused our attention on serious inequalities and the need for activism, so does *Lost Voices* force us to recognize the needs of children and adults with ME and to join the fight for a cure.'

The introduction to **Lost Voices** is an invaluable asset for anybody who has ever tried to answer the question 'What is ME/CFS?' It examines some key areas of confusion which have resulted in misconceptions and ignorance about the nature and severity of the illness amongst the general public, the government and the medical profession. Cutting through this misunderstanding, the introduction to **Lost Voices** argues powerfully for a new biomedical focus on subgroups to drive future ME/CFS research and treatment.

Lost Voices is a book to help others understand the hidden reality of life with severe ME; a book that allows one to feel the comfort of shared experience whether it be suffering, courage, love, hope or determination; a book with key information about ME; a book to be moved by; a book to enjoy.

Please buy Lost Voices and use it to help fight the ignorance and injustice that results in so many ME sufferers struggling invisibly and unheard.

The purpose of this book is to educate in the broadest possible sense and it is not being sold for profit by Invest in ME."



Conference Edition Editorial Comment

Welcome to the 2009 conference edition of the Journal of IiME – a blend of science, facts, stories and news regarding Myalgic encephalomyelitis (ME or ME/CFS). May is ME Awareness Month and also the month when Invest in ME hosts its annual biomedical research conference. It is an apt time to look back at what has occurred in the last year as well as to look forward to future developments. In the year which has elapsed since our 2008 conference some events have occurred which will have consequences for people with ME and their families, for researchers and health services when it concerns ME. These events are a mixture of regret, disappointment, anger but also progress and hope.

The last year has seen the NICE guidelines for ME being promoted and, some would argue, forced upon the health services and unwilling patients.

The dissatisfaction with the NICE guidelines has seen a patient revolt and NICE, yet again, being taken before a Judicial Review to defend its processes and its decisions by the very patients it was meant to protect and to treat.

A major criticism of NICE is that it failed to look at the established, published biomedical research and instead produced a document which is neither helpful for patients nor useable by medical professionals. Its scope, based on flawed input, was also far too narrow to make any meaningful difference.

One of the most disappointing aspects of the Judicial Review was the spectacle of NICE

attempting to paint these guidelines as a "gold standard". This risible self-assessment by NICE showed a flawed organisation which needs overhauling.

Another organisation failing people with ME has been the Medical Research Council. The last eighteen months has witnessed the UK Medical Research Council officially acknowledge that its previous policy toward ME research has been an abject failure by setting up a new panel to look at research into ME.

There is doubt of the genuineness of the MRC to seriously change its approach. The criticism which IiME has of this panel is that it includes some who wish to reclassify, or who perceive ME as a behavioural illness and this undermines the reason for this panel's existence and its continued operation.

With its usual tardiness the MRC has spent eighteen months since the panel's inception and has yet to produce anything of substance. We would suggest to the MRC that the patient community might have far greater involvement in this panel than it currently allows. We also believe that the eventual decision-making process of subsequent research proposals by that panel and any peer reviewers must be completely transparent – something the MRC continues to fail to do and which has seen obvious bias in funding of research into ME in the past.

The need to sub group ME patients to allow proper research and treatments was

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.

Comment

highlighted at our last conference and from there we move on this year to focus on severe ME.

The severely affected are a group of patients who do not figure often in research – which may be due to the lack to appropriate funding.

The severely affected people with ME are neglected by healthcare organisations and by the establishment authorities responsible for funding research. Many believe it is only by examining severely affected patients that the true nature of this illness is revealed and treatments and cures will be found.

Appropriately, to coincide this year with our emphasis at the conference on severe ME Invest in ME has published the Lost Voices book – a unique collection of stories, photographs and facts which highlights the effect of severe ME on patients, on families and on society. Lost Voices has already been distributed to twenty countries and is to be found in medical libraries, community libraries, hospitals, GP surgeries, and a whole raft of various places within the community.



Since the last Invest in ME international biomedical research conference the European ME Alliance (EMEA) has also been created and meets in London after the conference for its first AGM. The Alliance now spans across Europe, the most recent addition being Spain, and it is hoped to supplement with the remaining European countries before long.

The Invest in ME conference in London in May will be our fourth biomedical research conference and now welcomes delegates from four continents and fourteen countries. We welcome many new delegates as well as old friends.

Some who will not be seen at the conference (as we go to press) will, again, be the Secretary of State for Health, the Medical Research Council and the Chief Medical Officer. Despite the persistence of liME in asking, and an amazing response from the ME community in petitioning, these main establishment areas still fail to take ME seriously enough to listen to the foremost speakers displaying research on their doorstep.

The sad point about this is that treatments are available for ME. The liME 2008 conference had presentations from Dr John Chia and Dr Martin Lerner, showing effective treatments for some sub groups of ME – treatments which NICE actually refused to endorse.

The fact that treatments by antivirals are currently expensive is seen as one reason why they are not used in the UK for ME. Yet the recent outbreak of swine flu has shown how easy it is to provide antivirals to anyone suspected of having contracted this strain of the flu virus.

Invest in ME have written to the Chief Medical Officer and asked why is ME any different? Are lives not worth more than money? Should not the Chief Medical officer be making a statement as to why antivirals (or any other relevant medications) are not used for ME? If only the CMO would accept one invitation to the liME annual biomedical research conference then he would be able to see first hand how this might affect real people.

In the absence of progress from the government, Medical Research Council and within the NHS we need a CMO who will stand up for patients.

We need action and leadership and we cannot afford to lose yet another generation to this illness.

Perhaps the next year will be different. liME will continue with our conferences and are already putting plans on paper for a bigger conference in 2010 to celebrate our fifth

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biomedical conference.

So let us take a hypothetical situation which occurs between our 2009 conference and leading up to our 2010 conference.

Let us suppose that a diagnostic test was developed and that sub groups were more easily able to be identified in order to guide treatments.

Let us suppose that the disease mechanism for ME was found?

How would ministers and healthcare officials react to such changes?

What changes would be seen in the healthcare system?

How would the pharmaceutical industry react when there is a promise of great rewards from development of effective treatments and possibly cures for ME based on successful biomedical research?

How would NICE react?

What changes in attitude would come forth from insurers and Work and Pensions departments toward the current policies where benefits are often denied to people with ME?

Would the CMO change his stance?

Would the Medical Research Council be more transparent and begin funding biomedical research based on sound science rather than on vested interests?

Would the MRC seriously allow funding of biomedical research to begin?

We believe that researchers such as those at our conference are making such enormous progress that we should be looking at the above scenario and begin to be prepared to ask these questions.

In the last year we have seen the great potential of biomedical research being realised due to the approach adopted by organisations that have a clear strategy – amongst them the Whittemore-Peterson

Institute. We feel the newly-established Enterovirus Foundation will also influence the progress of biomedical research into ME.

Invest in ME has, since its inception, been advocating a national strategy of biomedical research into ME as the only logical way forward. However, this is now being superseded by the requirement for an international strategy of biomedical research. The WPI and the researchers at our conference are making great strides in progress and Invest in ME wish to publicise their work at every opportunity and encourage people around the world to support them – both in moral and financial support.

After the conference Invest in ME will be working with our European colleagues to further the establishment of centres similar to the WPI.

Our Biomedical Research Fund, announced, in January, will be used to help with this and provide a focal point for these plans.

We can hope that by our next conference in 2010 the landscape might have changed significantly enough so that we will be reporting on progress on this development and talking of a year of success. For next year's conference we hope to be welcoming more new delegates – including those who are currently conspicuous by their continuing absence.

And so to the Journal.

Appropriately, to reflect the emphasis on severe ME at the conference we have several articles revolving around severe ME. Following the death of Alison Hunter from complications arising from ME the Alison Hunter Memorial Foundation (AHMF) of Australia was set up by her mother, Chris. Chris Hunter has given us permission to republish a very moving article by Alison – written many years ago but as relevant today as it was when Alison wrote it at the age of 17 – a story which any parent of a child with ME would

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today immediately recognise and which could have come directly from this year's Lost Voices book.

How does it feel when a local health authority fails to provide a biomedical clinical lead for severe ME patients even though it is possible? We have the views of one severely ill patient on this situation.

The story of the Krisner family of Norway was highlighted on our 2006 conference DVD – a story of devastating consequences for a family where three siblings have become ill with severe ME. Yet there is hope. After continuing treatment two of the children are making amazing progress and the other has made some improvement. Kjersti and Harald Krisner provide an article showing this progress – a story of great progress and hope.

The new Enterovirus Foundation has been created and we welcome members of the EVF, Professor Steven Tracy and Nora Chapman, who have provided an excellent article on Human Enteroviruses and Chronic Infectious Disease.

Dr John Chia, who is speaking at our conference, is part of the EVF.

We have two papers from Professor Garth Nicolson et al – one showing the similarities between CFS (ME) and Autism Spectrum Disorders and the other discussing weight issues with CFS (ME) and the use of an all natural oral supplement mixture.

Epidemics are a less well publicised feature with ME. Professor Harald Nyland will be talking about this at the conference yet epidemics are not new. The Incline village episode in the eighties is responsible for some of the foremost ME researchers continuing their work.

We have an old article on epidemics from Dr Gordon Parrish which we felt was worthy of being republished to put the work of today's researchers into context.

We also include conference abstracts.

Invest in ME wish to thank those organisations

and individuals who have donated or sponsored to enable us to bring about the 4th Invest in ME International ME/CFS Conference 2009. Thank you for your generosity.

We would like to thank the Irish ME Trust and the Alison Hunter Memorial Foundation for their donations, support and friendly cooperation.



To those who attend the conference we hope you enjoy your day and learn a great deal. For those not able to come to the conference then we hope the Journal will provide something of use. The conference promises to reflect the real progress which is finally beginning to benefit people with ME despite being enacted on a background of terrible suffering and intransigence of those responsible for deciding healthcare policy.

Enjoy the Journal, enjoy the conference.

ME FACTS

The US Centres for Disease Control (CDC) website confirms that:

"The name ME was coined in the 1950s

to clarify well-documented outbreaks of disease; ME is accompanied by neurological and muscular signs

(sic) and has a case definition distinct from that of CFS(ME)".

(<http://www.cdc.gov/cfs/cme/wb1032/chapter1/overview.html>).

SEVERE ME – A PATIENT'S VIEW

Severe ME requires investigation and treatment by biomedical researchers and clinicians understanding the biomedical basis for the illness.

**Against a background of severely affected people with ME facing reluctance from healthcare authorities to consider their future, then when a health authority has an opportunity to employ world-renowned researchers and physicians who understand the illness, when a patient community is pleading with the same health authority to employ these same physicians, then any logical person must ask why isn't this happening?
Here a long time sufferer of ME has dictated the following article.**

I want you to imagine what it is like to have severe, neurological ME.

I want you to try and think what it must be like to experience constant ongoing physical pain, all over your whole body. Pain that throbs, pain that stings, pain that itches and irritates, burns and moves, pain that invades your muscles, your skin, your scalp, your feet, your eyeballs, your tongue, your intestines, so that there is no part of you experiencing any respite from pain, any second of the day or night, in fact the pain increases in intensity and agony every time you try to rest or sleep.

I want you to try and imagine muscle paralysis that invades you, so that when you awake you can no longer speak, move your lips open your mouth, open your eyes, move your fingers, feel your hands or your arms, your feet, your toes, your legs.

I want you to imagine what its like to desperately need to go to the toilet but to be unable to move, to be unable to sit or stand, to be unable to walk but worse than this to be unable to bear to be touched. So that even if there is someone to move you, to lift you, to stand you up, to sit you in a wheelchair, to push you to the bathroom, you cannot access this help.

Day upon day, year upon , year for hours on end.

I want you to imagine the physical torment of hyperacusis, of being so hypersensitive to noise that a whisper sounds like a shout and that any loud noise feels like a physical assault not just on your ears and your head but on your whole body.

I want you to imagine the ordinary things of life becoming completely inaccessible because you have no energy, you cannot breathe easily or fully, you cannot eat so many different foods because of allergy and sensitivity, you cannot be in the same room as people because they drain you of any energy you might have had and their voices hurt you and you become more ill if you try to engage with them.

I want you to imagine a life where the TV hurts your eyes, where the computer screen hurts your eyes, the sunlight, even the normal daylight, without bright sun, hurts your eyes and gives you severe eye pain.

A head pain that goes on and on for days on end.

A life where the telephone hurts you to hold it, to hear it and where your brain is unable to process any incoming information rendering

SEVERE ME – A PATIENT'S VIEW

conversation impossible.

I want you to imagine being unable to read because your brain simply is unable to comprehend the mass of information before you; of being unable to imagine, even, because the fog has descended inside your head that blanks out thought and creativity ability.

This is only a portion of the reality of having severe ME.

Now I want you to think what it must be like to know that despite this severe disability, this chronic unending illness:

- There is no biomedical consultant provided to treat you
- There is no apparent awareness of the urgent need to do something to physically help you
- There is no NHS service offering appropriate biomedical tests or treatments despite the fact there are very serious physical abnormalities in your body and every time you ask for help you are sidelined
- Every time you try to raise awareness it doesn't make any difference.

What must it be like then to find that there is an opportunity for world class, concerned and interested medical consultants – consultants who know your illness is a physical reality, one that has been grossly neglected, - who actually want to come and provide a new service, to right the injustice of no appropriate medical provision in your area ?

Can you begin to imagine what it feels like when, instead of this offer being accepted, you are fobbed off instead with a biopsychosocial, therapy-led service (pretending to be biomedical) that

does not meet the complex medical needs of this disease?

When all the PCT has to do is say -

"Yes",

"we will take you seriously" ,

"We acknowledge responsibility for your biomedical care",

"we can see that you need a local consultant and it is not unreasonable to expect one;"

"So yes, we will provide you with a new innovative biomedical service that might just begin to meet your needs.."

"And we will lead the way."

Please tell me why this is not happening ?

ME FACTS

In 1988, UK researchers Archard and Bowles et al published the results of their research into muscle abnormalities in ME/CFS:

"These data show that enterovirus RNA is present in skeletal muscle of some patients with postviral fatigue syndrome up to 20 years after onset of disease and suggest that persistent viral infection has an aetiological role. These results provide further evidence that Coxsackie B virus plays a major role in ME, either directly or by triggering immunological responses which result in abnormal muscle metabolism"

(JRSM 1988;81:325-331).



Somewhere in the recesses of my mind there is a memory of being active, of having the energy to be active...when sprinting across the street was a reflex action and a good day was a day in the surf followed then by dinner at a new restaurant followed by a movie.



There was a time when my body parts just existed... now, they ache as if to remind me of their presence. "Yeah boys, how you doin', still there, GREAT." An average day now consists of showering (with a seat), getting dressed, and perhaps a few hours of study interspersed with hours on the horizontal.

The fatigue is not everyday tiredness, experienced after an energetic day's gardening. It is an exhaustion of body and mind so profound that it becomes a concerted effort to think, walk and sometimes even move, sit, eat or breathe. Arms and legs turn to lead; they sink through the mattress to eternity...there is often pain throughout the body which can be constant and localised (for e.g. continual severe headache) or migratory...calf muscles one day, finger joints the next. Then there is nausea, diarrhoea, ringing in the ears...

Aside from the physical problems there are the cognitive symptoms (the memory loss, the lack of concentration) alongside the neurological: the dizziness and sensitivities to extremes of temperature, light and noise.

Doctors have at last pinpointed the mechanism by which such signs occur - lack of blood flow to

This poignant article is as relevant today as when it was written by Alison in September 1993. It has been reproduced here by kind permission of the Alison's mother Chris Hunter.

The Alison Hunter Memorial Foundation

The Alison Hunter Foundation was established in 1998.

The Foundation is an enduring memorial to Alison Hunter and all those whose lives have been devastated by ME/CFS.

Alison died in 1996, aged 19, from complications arising from ME/CFS which included seizures, paralysis, gastrointestinal paresis and overwhelming infection resembling Behcets Disease.

Such complications are rare and only present in a severe subgroup.

Alison courageously fought ME/CFS for ten years and was an unstinting advocate for young people.

The Alison Hunter Memorial Foundation is a non-profit institution. The Foundation works independently in a spirit of support and cooperation with all researchers, institutions and ME/CFS societies to advance scientific knowledge and medical care.

<http://www.ahmf.org/>

certain areas of the brain. Little comfort when at the age of 18, one finds oneself unable to remember one's home address, misspelling or mispronouncing basic words or walking into a room with no recollection of why or how.

"How are you?" is a question I'm asked all the time; every day almost by friends, family. Most

Forget M.E. Not (continued)

people don't really want to know; it's a form of etiquette, and usually a customary "Okay" or "Not too bad" fits the bill. "Not too good", on the other hand, or (heaven forbid) "Quite unwell" is met with a look that says, "Whaddaya mean?!" I have breached the unwritten code of greeting...awkward silence ensues.

Admittedly, many don't even listen to the reply: "How are you?" "Not feeling at all well." "That's great, did you see the movie on Channel Nine last night?"

A big problem is that aside from pallor I generally look healthy enough...a problem, because one loses credibility when one doesn't conform to the 'sick stereotype'—supposedly thin, frail and slow moving—and are predisposed to comments like "How can YOU be sick, you don't look at all sick?"



With a disease lacking a diagnostic test everyone's an expert...everybody knows someone's niece or cousin twice removed who went to see Dr So-and-so and now she's climbing mountains. Each new regime might be 'the One' to set things moving in the right direction. They stretch from the sublime to the ridiculous but you must try them all lest "don't you ever want to recover?"

These treatments aren't always benign, leaving you worse off than when you started, not to mention emotionally and financially.

Seven years down the track there's nothing I haven't tried: Chinese herbs, positive thinking, acupuncture, positive thinking, dietary manipulation, positive thinking, aromatherapy, positive thinking, electromagnetic therapy, all the while thinking positive because, "With a positive attitude you're almost there." Well,

thinking negative certainly doesn't help, but remarks such as "Chin up", "Look on the bright side", "There are many people worse off than you" only serve to alienate. Surely for a person to be cheerful all the time given the pain level, lifestyle restrictions etc would be a cause for concern.

Should these treatments fail it is invariably because you didn't have the right attitude, because "Mrs Jones tried it and hasn't looked back", a mentality accurately summed up as 'wellness macho'.

We present a challenge to doctors...if they know us well they believe we are ill but are at a loss as to how to help...most patients aren't so lucky and are labelled neurotic, school phobic, anorexic, menopausal, hypochondriacal, and are handed a referral to see friendly Mr — to have a little chat about why we need to be sick. This is extremely damaging.

However even the most understanding doctor becomes frustrated when tests repeatedly come back 'normal'. They cannot give us a pill to make it (and us) go away, and worsening health drives us back again and again in desperation to ask, "Doctor, can't you do something??"

Rarely will they say, "I don't know what is wrong with you", which they see as incompetence, when in fact the patient already realises this, and is far preferable to yet another blame-the-patient technique.

For pain, other than strong medication, distraction therapy wards off insanity in desperate moments, be it gentle massage, an engaging comedy, company, laughter...distraction as a form of pain relief has been known from centuries such as this quite probably effective (if outmoded) example found in the *Oxford Concise Medical Dictionary*: "A seton is a skein of cotton or the like passed below skin and left with ends protruding to maintain an artificial issue as a counter irritant."

Forget M.E. Not (continued)

Having missed altogether four years of schooling I may not have received a formal education, nevertheless I have learnt many invaluable 'life lessons' I don't believe are to be found between classroom walls, for example tolerance, empathy and open-mindedness. I don't hold much with the enriched sufferer theories however: "Great, I've suffered unrelenting pain for seven years, but I'm gonna be a better citizen."

Books, newspapers, radio and some television programs...these have been my umbilical cord to outside life, a world I often don't feel a part of. I have reached the conclusion that should be a number one priority although it is generally taken for granted, even by me; in the rare instances I catch a glimpse of it, feel the energy in my fuel tank, I am like a compulsive spender, spending the last drop plus more until I am back in bed. In my world you pay for your fun.

Sometimes it is worth it—often it isn't; we have no problem with motivation; quite the opposite, we are our own worst enemies.

My family have been wonderful, after all an illness like this impacts upon every member...Mum's had to give up work temporarily, no more spontaneous family holidays, siblings take a back seat.

It's hard being a teenager, trying to assert your individuality while so forcibly dependant on people for practical care. Of prime importance to adolescents is the need to feel accepted, normal, "one of the pack".

This is impossible to achieve when you mysteriously disappear every day after recess, receive extensions on assignments and have to decline invitations to most parties, sporting activities etc.

I am lucky to have a few "healthy" friends who are supportive and as understanding as they can be, who visit when I am bedbound and no longer ask if I'd like to go on interstate hikes.

I also have strong friendships with adolescents

with the same illness—we can provide mutual support & encouragement...most of all we can 'Lounge Lizard' together.

When you are chronically ill, you tend to lose your identity to the illness; it defines who you are and what you are capable of...particularly in other people's perceptions.

Sometimes I'm tempted to yell, "What about me the person?" I have thoughts and feelings aside from those associated with the illness, if not the opportunity, nor indeed the energy, to express them.

All the normal adolescent turmoil is experienced, perhaps magnified and without resolution, for how do we assert our individuality if not through experiencing life and interacting with a wide variety of human beings...certainly not lying in bed, doing the rounds of specialists once again, just in case, just to make sure they didn't miss something "fixable".

For years I was going to be "all better next week". Now I know better, I know the statistics and am aware that I have moved into the so-called chronic stage with little chance of spontaneous remission.

A cure may be just around the corner but I have to face the fact that I may be sick for a long time yet.

It's not AIDS, although it's similar, you can feel equally as ill only it doesn't kill you. Not cancer either. I'm not dying or anything drastic like that. It's M.E. Don't forget M.E.



Similarities of Chronic Fatigue Syndrome (CFS) and Autism Spectrum Disorders (ASD): Comparisons of Co-Infections

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The 4th Invest in ME International ME/ Chronic Fatigue Syndrome Conference in London, UK, May 28-29, 2009.

ABSTRACT

Objective:

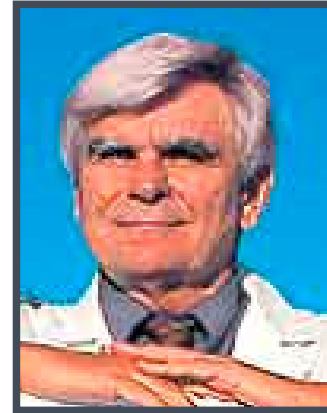
The majority of neurodegenerative diseases, fatiguing illnesses and neurobehavioral disease patients have chronic infections. Therefore, we examined the presence of certain co-infections in the blood of patients with Autism Spectrum Disorders (ASD) and compared these to CFS patients.

Methods:

North American CFS and ASD patients were examined for various infections by isolation of leukocyte blood fractions and forensic polymerase chain reaction (PCR) to determine various infections.

Results:

CFS patients (n=100, age=39.7±8.9) show evidence of multiple, systemic infections (Odds Ratio = 18.0, 95% CL 8.5-37.9, p< 0.001) that may be important in CFS morbidity. CFS patients had a high prevalence (51%) of 1 of 4 *Mycoplasma* species (OR = 13.8, 95% CL 5.8-32.9, p< 0.001) and often showed evidence of co-infections with different *Mycoplasma* species, *Chlamydia pneumoniae* (OR = 8.6, 95% CL 1.0-71.1, p< 0.01) and/or active Human Herpes Virus-6 (HHV-6) (OR = 4.5, 95% CL 2.0-10.2, p< 0.001). We found that 8% of the CFS patients showed evidence of *C. pn.* and 31% of active HHV-6 infections. Recently we examined ASD patients (n=48, age 8.4±2.8) and found a large subset (58.3%) of ASD patients showed evidence of *Mycoplasma* species infections compared to age-matched control subjects (OR = 13.9, p<0.001). ASD patients also had *C. pn.* (4/48 or 8.3% positive, OR = 5.6, p<0.01) and HHV-6 (14/48 or 29.2%, OR = 4.5, p<0.01) infections in their blood.



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Conclusions:

The results indicate that similar to CFS patients a large subset of neurobehavioral (ASD) disease patients show evidence of chronic infections. Although there were significant differences in median age and diagnoses between the two groups of patients, they tended to have similar incidence of three types of chronic infections: *Mycoplasma*, *Chlamydia* and HHV-6.

Similarities of ME/Chronic Fatigue Syndrome (ME/CFS) and Autism Spectrum Disorders (ASD): Comparisons of Co-Infections

(continued)

INTRODUCTION

Although no single underlying cause has been established for CFS, there is growing awareness that CFS can have an infectious nature that is either causative for the illness, a cofactor for the illness or appears as an opportunistic infection(s) that aggravate patient morbidity (1, 2). There are several reasons for this, including the nonrandom or clustered appearance of CFS, sometimes in immediate family members (2-4), the presence of certain signs and symptoms associated with infection, the often cyclic course of the illness and its response to antimicrobial therapies (2, 5, 6).

Previously we found that Gulf War veterans with CFS-like illnesses and a positive test for *Mycoplasma fermentans* transmitted their infections to their spouses and children (4). The adults in these families were diagnosed with CFS (7) but the children were subsequently diagnosed with Autism Spectrum Disorders (ASD) (8). The criteria for diagnosis of ASD are, in general terms, the presence of a triad of impairments in social interaction, communication and imagination (9).

Examination of ASD patients in civilian families for the presence of *Mycoplasma* species infections revealed that the majority of these patients had one or more infections (10).

In ASD cases there are reports of nonspecific signs and symptoms similar to those seen in CFS, such as fatigue, headaches, gastrointestinal and vision problems and occasional intermittent low-grade fevers and other signs and symptoms that are generally excluded in the diagnosis of ASD. These suggested to some authors that a subset of ASD patients may suffer from bacterial or viral infections (11). Here we examined three commonly found systemic infections in CFS patients, *Mycoplasma* species, *Chlamydia pneumoniae* and HHV-6 (12-14) and compared the incidence to the same infections found in ASD patients (10).

MATERIALS AND METHODS

Patients: All CFS patients (North American, n=100) underwent a medical history, completed a sign/symptom illness survey, had routine laboratory tests and met the Fukuda et al. (15) exclusionary criteria. Control subjects (n=100) had to be free of disease for at least three months prior to data collection, and they had to be free of antibiotic treatment for three months prior to blood collection. All ASD patients (N=48) were randomly recruited from patient support groups in California after diagnosis of ASD according to the *International Classification of Diseases* (ICD-10) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV). All ASD patients were assessed by the Autism Diagnostic Interview-Revised (ADI-R) (16) and Childhood Autism Rating Scale (CARS) (17, 18). Most (45/48) had a diagnosis of autism, while 6/48 were diagnosed with ADD (three of which were also diagnosed with autism) and nine autism patients with Asperger's Syndrome.

PCR Analysis of Blood:

Blood was collected in EDTA-containing tubes and immediately brought to ice bath temperature as described previously (12-14). Samples were shipped with wet ice by overnight air courier to the Institute for Molecular Medicine for analysis.

All blood samples were blinded. Whole blood (50 µl) was used for preparation of DNA using Chelex (Biorad, Hercules, USA). Aliquots from the centrifuged samples were used immediately for Polymerase Chain Reaction (PCR) as described previously (12-14).

Statistics:

Subjects' demographic characteristics were assessed using descriptive statistics and students' t-tests (independent samples test, t-test for equality of means, 2-tailed). The 95% confidence interval was chosen for

Similarities of ME/Chronic Fatigue Syndrome (ME/CFS) and Autism Spectrum Disorders (ASD): Comparisons of Co-Infections

(continued)

minimal significance. Odds Ratios were calculated using logistic regression (Logit method) Statistica 5.5 (Statsoft, Tulsa, OK). In some cases, Pearson Chi-Square test was performed to compare prevalence data between patients and control subjects.

Bacterial and Viral Infections:

Using the blood of CFS patients (n=100) and PCR procedures an overwhelming majority of patients showed evidence of multiple, systemic bacterial and viral infections (Odds Ratio=18.0, $p<0.001$).¹⁷ CFS patients had a high prevalence (51%) of one of four *Mycoplasma* species (Odds Ratio=13.8, $p<0.001$) and often showed evidence of co-infections with different *Mycoplasma* species, *C. pneumoniae* (8%, Odds Ratio=8.6, $p<0.01$) and active HHV6 (30%, Odds Ratio=4.5, $p<0.001$) (Table 3).

Evidence for *Mycoplasma spp.* infections was found in 28/48 or 58.3% of ASD patients and

RESULTS

Patient Demographic Data: These are shown in Tables 1 and 2.

TABLE 1. CFS Patient demographic data.

	n	Mean age (SD)	Range	Males (%)	Females (%)
Patients	100	39.7 (8.9)	18-66	28 (28)	72 (72)
Controls	100	34.6 (9.1)	21-58	31 (31)	69 (69)
Female patients	72	39.8 (9.8)	18-66	0 (0.0)	72 (100.0)
Male patients	28	39.2 (10.3)	20-60	28 (100.0)	0 (0.0)

TABLE 2. ASD Patient demographic data.

	n	Mean age (SD)	Range	Males (%)	Females (%)
Patients	48	8.4 (2.8)	3-14	36 (75)	12 (25)
Controls	45	7.9 (3.3)	4-11	28 (62.2)	17 (37.8)
Rural patients	18	8.1 (2.9)	3-14	14 (77.7)	4 (22.3)
Urban patients	30	8.6 (3.2)	4-14	22 (73.3)	8 (26.7)

Similarities of ME/Chronic Fatigue Syndrome (ME/CFS) and Autism Spectrum Disorders (ASD): Comparisons of Co-Infections

(continued)

TABLE 3. Prevalence and Odds Ratio Analysis of Systemic Infections Between 100 CFS Patients and 100 Healthy Control Subjects.

Type of infection	CFS Patients n = 100	Control Subjects n = 100	Odds Ratio, 95% CL, p or Chi ²
Number Infected	71	12	18.0 , 8.5-37.9, p< 0.001
HHV-6	31	9	4.5 , 2.0-10.2, p< 0.001
<i>C. Pneumoniae</i>	8	1	8.6 , 1.0-71.1, p< 0.01
<i>Mycoplasma</i> spp.	51	7	13.8 , 5.8-32.9, p< 0.001
<i>M. pneumoniae</i>	29	3	13.2 , 3.8-45.4, p< 0.001
<i>M. fermentans</i>	22	2	13.8 , 3.1-61.1, p< 0.001
<i>M. hominis</i>	16	1	18.8 , 2.4-147.0, p< 0.001
<i>M. penetrans</i>	8	1	8.6 , 1.0-71.1, p< 0.01
Single mycoplasmal infection	29	7	13.8 , 5.8-32.9, p< 0.001
Multiple mycoplasmal infections	22	0	Chi ² = 24.7 , p< 0.001
<i>M. fermentans</i> + <i>M. pneumoniae</i>	10	0	Chi ² = 10.5, p< 0.001
<i>M. fermentans</i> + <i>M. hominis</i>	7	0	Chi ² = 7.3, p< 0.007
<i>M. pneumoniae</i> + <i>M. hominis</i>	3	0	Chi ² = 3.1, p< 0.08
<i>M. fermentans</i> + <i>M. hominis</i> + <i>M. pneumoniae</i>	2	0	Chi ² = 2.0, p= 0.16
<i>Mycoplasma</i> + HHV-6	16	0	Chi ² = 17.4 , p< 0.001
<i>Mycoplasma</i> + <i>C. pneumoniae</i>	4	0	Chi ² = 4.1, p< 0.04
<i>C. pneumoniae</i> + HHV-6	3	0	Chi ² = 3.1, p< 0.08

2/45 (4.7%) age-matched control subjects (Odds Ratio=13.8, p<0.001) (Table 4). *C. pneumoniae* infections were found in 4/48 or 8.3% of ASD patients and in 1/45 or 2.1% of control subjects (Odds Ratio=5.6, p< 0.01) (Table 4).

We also examined the incidence of HHV-6 infections in ASD patients and found that 14/48 or 29.2% of ASD patients were positive compared to 4/45 (8.8%) positives in age-matched control subjects (Odds Ratio=4.5, p<0.01). We did not find any multiple co-infections in control subjects. The differences between infections in ASD patients and control subjects were highly significant (Odds Ratio=16.5, p< 0.001). Significant differences were not found in the prevalence of infections in urban and rural patients, in male or female patients or between autism and other ASD diagnoses.

DISCUSSION

In contrast to the ASD children in military families where primarily one species of

Similarities of ME/Chronic Fatigue Syndrome (ME/CFS) and Autism Spectrum Disorders (ASD): Comparisons of Co-Infections

(continued)

TABLE 4.

Prevalence and Odds Ratio Analysis of Systemic Infections in ASD Patients and Matched Healthy Control Subjects.

Type of infection	ASD Patients n = 48 (%)	Control Subjects n = 45 (%)	Odds Ratio, p or Chi ²
HHV-6	14 (29.2)	4 (8.3)	4.5 , p< 0.01
<i>C. Pneumoniae</i>	4 (8.3)	1 (2.1)	5.6 , p< 0.01
<i>Mycoplasma</i> spp.	28 (58.3)	2 (4.7)	13.8 , p< 0.001
<i>M. pneumoniae</i>	16	2	9.2 , p< 0.001
<i>M. fermentans</i>	17	0	14.8 , p< 0.001
<i>M. hominis</i>	5	0	11.8 , p< 0.01
<i>M. penetrans</i>	1	0	6.6 , p< 0.01
Single mycoplasmal infection	16 (33.3)	2 (4.7)	13.8 , p< 0.001
Multiple mycoplasmal infections	12 (25.0)	0 (0)	Chi ² = 11.7 , p< 0.001
<i>M. fermentans</i> + <i>M. pneumoniae</i>	7	0	Chi ² = 4.7, p< 0.01
<i>M. fermentans</i> + <i>M. hominis</i>	2	0	Chi ² = 1.9, p< 0.3
<i>M. pneumoniae</i> + <i>M. hominis</i>	1	0	Chi ² = 1.4, p< 0.2
<i>M. fermentans</i> + <i>M. hominis</i> + <i>M. pneumoniae</i>	2	0	Chi ² = 1.9, p<0.2
<i>Mycoplasma</i> + HHV-6	8 (16.7)	0 (0)	Chi ² = 4.4 , p< 0.01
<i>Mycoplasma</i> + <i>C. pneumoniae</i>	2 (4.2)	0 (0)	Chi ² = 2.1, p< 0.19
<i>C. pneumoniae</i> + HHV-6	1 (2.1)	0 (0)	Chi ² = 1.6, p< 0.3

Similarities of ME/Chronic Fatigue Syndrome (ME/CFS) and Autism Spectrum Disorders (ASD): Comparisons of Co-Infections

(continued)

Mycoplasma was found (usually *M. fermentans*), the majority of ASD patients in Central California were found to have single or multiple mycoplasmal infections involving *M. pneumoniae*, *M. fermentans*, *M. hominis* or *M. genitalium*. We also examined two other commonly found infections in CFS patients (4-7), *C. pneumoniae* and HHV-6 (13, 14).

The results suggested that infections are a common feature in ASD as well as CFS. Consistent with this hypothesis is the finding that autism occurs at greater prevalence during periods of more frequent hospitalizations for bronchitis or pneumonia (19), and maternal viral infections during the second trimester of pregnancy are associated with increased risk of autism in their offspring (20, 21).

In a separate study on CFS patients the presence of chronic infections has also been statistically related to the number and severity of signs/symptoms seen in CFS patients (14).

Although similar studies in ASD patients have not been done, it has been observed that patients with severe ASD are those with systemic infections of the type seen in this study (unpublished observations).

The appearance of infections in children diagnosed with ASD may eventually be linked to the multiple vaccines received during childhood either as a source or from opportunistic infections in immune suppressed recipients of multiple vaccines. Although the etiology of ASD is currently unknown and thought to involve both genetic and environmental factors (22, 23), the infections found in ASD patients should be considered along with other factors in the management of these disorders (24).

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ME FACTS

In many of the published studies, graded exercise therapy has been adopted as a component of the CBT programme (i.e. graded exercise was used as a way to diminish avoidance behaviour towards physical activity).

Unfortunately, the studies examining the effectiveness of GET/CBT in ME/CFS did not use musculoskeletal pain as an outcome measure (and) none of the studies applied the current diagnostic criteria for ME/CFS.

From a large treatment audit amongst British ME/CFS patients, it was concluded that approximately 50% stated that GET worsened their condition.

Finally, graded exercise therapy does not comply with our current understanding of ME/CFS exercise physiology.

Evidence is now available showing increased oxidative stress in response to (sub)maximal exercise and subsequent increased fatigue and post-exertional malaise

- Belgian researchers Nijs and De Meirleir (Manual Therapy 2006: Aug. 11(3):187-189).

A Researcher's View from the Whittemore-Peterson Institute



WHITTEMORE PETERSON
INSTITUTE FOR NEURO-IMMUNE DISEASE

I was originally exposed to the world of CFS research, while taking a class in Biostatistics, as an undergraduate.

My professor was a patient of Dr. Daniel Peterson and she approached him with the idea to conduct a research project using his CFS patient data, to which he agreed. Although the semester ended prior to completing the work I continued with the project on my own and ultimately we determined the value of CD4/CD8 ratios in diagnosing CFS and published and presented these data at the meeting of the American Mathematics Society in Eugene Oregon. It was during this time that I became acquainted with several CFS patients and truly understood their frustration regarding the lack of quality CFS research.

I continued to work with Dr. Peterson on an informal level conducting other research but eventually I left the Tahoe area and began my Graduate work at Temple University. After a short time on the East Coast things took me in a different direction and I found myself back in Nevada. Shortly after returning I entered Graduate school at the University of Nevada, Reno and that is where I concluded my Graduate work, receiving a Ph.D. in Biochemistry in 2006.

Although my Graduate work was conducted in Neuropeptide chemistry, I never lost contact with the CFS community and my desire to help the patients drew me back into the field; to this day I continue the work that started many years ago in the medical office of Incline Village.

Although there are many directions a new investigator can take when he or she decides what area of research to pursue, ultimately, my decision was most greatly influenced by the CFS patients I met in Dr. Peterson's office. I often imagined what it must be like to have a disease where the cause is unknown, the treatment is dubious and the mainstream medical community questions the validity of your disease.

With this thought in mind it was an easy decision to continue down the path of CFS

Dr. Vincent Lombardi



Dr. Lombardi was introduced to the field of ME/CFS as an undergraduate research assistant for Dr. Daniel L. Peterson, in Incline Village, NV. While working with Dr. Peterson, he was responsible for routine laboratory work, patient interviews, statistical and epidemiological data analysis. He began his graduate studies in the laboratory of Dr. Robert Suhadolnik at Temple University in 1999 studying the role of RNase L dysfunction in ME/CFS. He finished his graduate work at the University of Nevada, Reno in the field of neuro-peptides and protein chemistry, receiving his PhD in Biochemistry in 2006.

research, even though the path is not always so easy.

I have never been the kind of person that takes the easy road but the patients appreciate my work and that is enough for me.

Invest in ME have a page of ways to help support the ME community, including the WPI in its important work.

**[http://www.investinme.org/helpus.htm#
Donate-to-the-WPI](http://www.investinme.org/helpus.htm#Donate-to-the-WPI)**

EDUCATIONAL MATERIAL from IiME



Invest in ME have available the full presentations from the International ME/CFS Conferences in London of 2008, 2007 and 2006.

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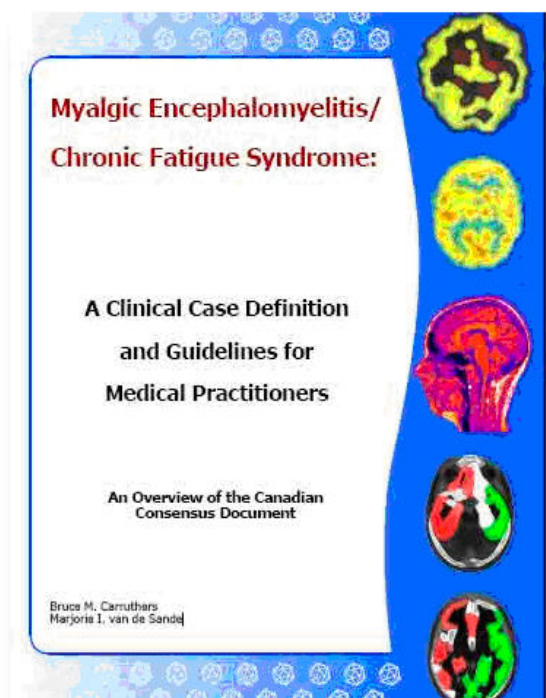
Canadian Guidelines

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

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

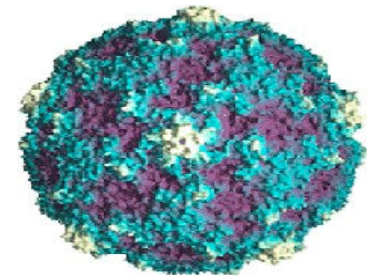
The Canadian Guidelines provide an internationally accepted means for clearly diagnosing ME The Canadian Guidelines are available from IiME and the price is 80p per copy plus postage & packaging.

To order please contact Invest in ME via this email address: info@investinme.org



Human Enteroviruses and Chronic Infectious Disease

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ABSTRACT

Most of what is known about human enteroviruses (HEV) has been derived from the study of the polioviruses, the HEV responsible for poliomyelitis. The HEV are generally not thought to persist for long periods in the host: an acute, sometimes nasty, infection is rapidly eradicated by the host's serotype-specific adaptive immune response.

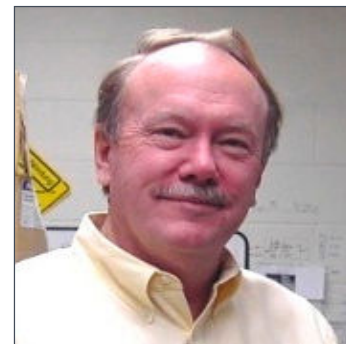
Our discovery that the commonly encountered HEV, the group B coxsackieviruses (CVB), can naturally delete sequence from the 5' end of the RNA genome and that this deletional mechanism results in long-term viral persistence, in the face of the adaptive immune response, has substantially altered this view.

This previously unknown and unsuspected aspect of enterovirus replication provides an explanation for previous reports of enteroviral RNA detected in diseased tissue in the apparent absence of infectious virus particles.

Introduction

The enteroviruses are an incredibly diverse and large genus in the family Picornaviridae. Within the enteroviruses, human enteroviruses (HEV; those which infect humans as opposed to other species) number at least 100 known serotypes, with more known to exist but which have just not been characterized to date. Serotype defines the virus: it is how the immune system recognizes the complex aggregation of proteins which makes up the virus particle or virion.

Thus, infection with one HEV serotype induces immunity that protects against disease which that HEV serotype might inflict upon one were the virus is encountered again, but this protective immunity does not extend to other serotypes. This is why the poliovirus vaccines work to protect from poliomyelitis: any



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Human enteroviruses and chronic infectious disease (continued)

subsequent infection with poliovirus is quickly suppressed by the pre-existing anti-poliovirus immunity and the virus infection eradicated. But of course, anti-poliovirus protective immunity does not protect from being infected with a different HEV.

Human enterovirus virions are small at 29nm in diameter; said another way, this means about 345,000 viruses would need to be lined up to equal one centimeter. The virus particle consists of an ordered array of 4 capsid proteins that forms an icosahedral structure of incredible beauty. In **Figure 1**, the reader can see what the coxsackievirus B3 (CVB3) virion would look like were one able to actually see it. This structure was solved with a technique called X-ray crystallography(23) in which X-rays, which are directed through crystals of virus and bent in specific ways, are then interpreted by computer analysis to provide a virus structure. Numerous other images of related enteroviruses can be found by visiting the website of the Institute for Molecular Virology at the University of Wisconsin in Madison WI, USA.

The HEV cause a plethora of different human diseases and syndromes, the most important of which are poliomyelitis [now largely, although not entirely, eradicated in the world through use of the vaccines(16)], meningitis and encephalitis, myocarditis, pancreatitis, myositis, and type 1 (insulin dependent) diabetes (T1D)(31).

Recent work has also indicated a possible role for HEV in the poorly understood etiology of chronic fatigue syndrome (CFS)(9, 11). Polio, T1D and CFS are noteworthy, in that these diseases are chronic and in the case of polio and T1D, fatal without treatment. Certainly, fatal cases of the other HEV diseases occur as well(28) but as a rule, HEV diseases are deemed to be acute illnesses of relatively low clinical importance because they are so common. Nonetheless, 5-10 million cases of symptomatic HEV infections occur annually in the US alone(27).

Group B coxsackievirus infection of the heart

Within only a few years after their discovery in

the late 1940s, the group B coxsackieviruses (CVB) were shown to be involved in inflammatory heart disease or myocarditis(6, 12, 32). Because of the ease with which the CVB replicated in mice, an experimental model to study myocarditis was soon available and has been exploited for numerous studies over the years. Once myocardial biopsy techniques became widespread as a clinical assay for the presence of myocarditis(29), researchers became interested in determining how often HEV was associated with myocarditis. These studies have demonstrated that about 15-20% of adult myocarditis cases can be associated with an HEV infection(2). This was carried out in most cases by isolating RNA from very small biopsy samples of the human heart, then analyzing the RNA for the presence of HEV RNA using a variety of techniques.

Interestingly, in those adult cases of myocarditis in which the presence of virus was shown by detecting the viral RNA, rarely can an infectious virus be isolated. This is confusing: how can one detect viral RNA and not detect the virus? And indeed, this was a conundrum for many years. Most HEV cause cells in culture to die; this outcome, termed cytopathic effect or cpe, is the result of the virus infecting the cells in culture and killing them in the process of producing the next virus generation. Failure to observe cpe upon inoculating cell cultures with homogenized heart samples, was taken to be evidence that virus *qua* virus was not present. This goes back to the foregoing discussion, in which the general view of HEV is as a virus that rapidly causes cell lysis (acute disease). As opposed to adult samples, samples of pediatric myocarditic heart tissue generally shows both the presence of cytopathic virus when placed in culture as well as the presence of viral RNA when molecular assays are carried out.

We considered the possibility that HEV infections of adult human hearts might generate a population of viruses that have been characterized and termed defective interfering (DI) viruses(10, 13). Although DI

Human enteroviruses and chronic infectious disease (continued)

Figure 1. Image of the coxsackievirus B3 (CVB3) virion derived from X-ray crystallographic studies (Mucklebauer and colleagues, 1995). This is shown looking directly at a two-fold axis of symmetry where everything above the middle of the image, left to right, is mirrored below. There are also 5 and 3 fold axes of symmetry. The arrow shows a 5 fold axis, around which can be seen 5 dark depressions called canyons, into which the host cell receptor protein can bind, thus initiating an infection of the cell by the virus. This and other images by Jean-Yves Sgro at the University of Wisconsin at Madison can be viewed online (see URL in the lower left). This image was generously supplied by J-Y. Sgro.

coxsackievirus B3
PDB ID: 1cov

Muckelbauer, J.K., Kremer, M.,
Minor, I., Tong, L., Zlotnick, A.,
Johnson, J.E., Rossmann, M.G. (1995)
Structure determination of
coxsackievirus B3 to 3.5 Å resolution.
Acta Crystallogr., Sect. D 51: 871-887

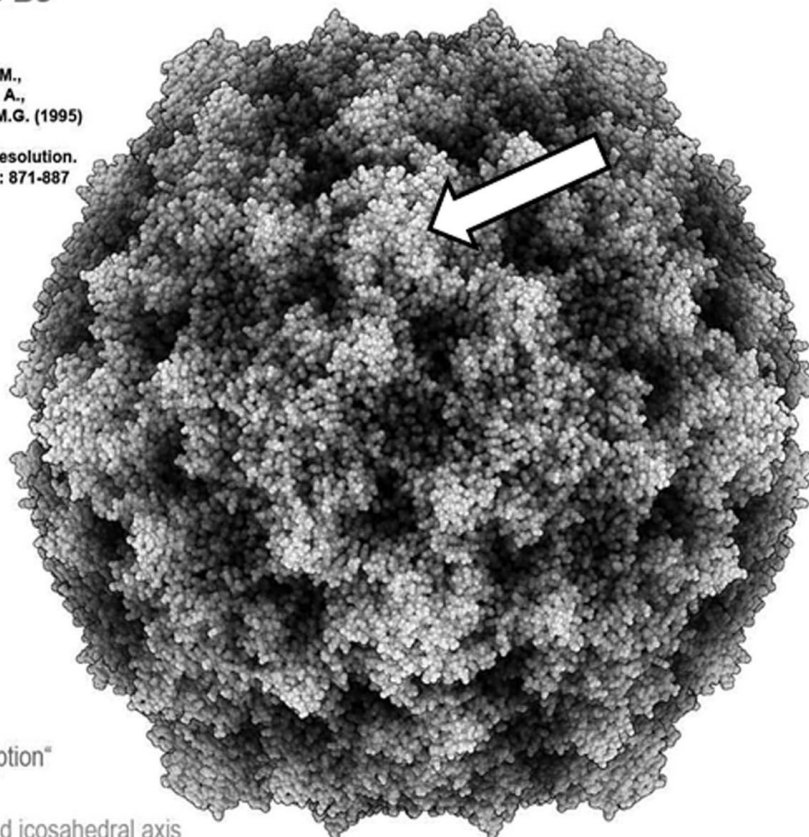
Quemol image by Jean-Yves Sgro ©2008
images at virology.wisc.edu/virusworld



20Å

"Shape Perception"

View along 2-fold icosahedral axis



Human enteroviruses and chronic infectious disease (continued)

HEV had never been demonstrated in humans or animals, they had been shown to exist in experimental cell culture and thus, the possibility that they might also exist in nature could not be excluded. Defective interfering HEV are viral RNA genomes that have deleted variable parts of the sequence that encode the capsid (coat) proteins of the virus (see **Figure 2**). This implies such viruses could never be successful, as they could never produce an intact virion. However, DI HEV exist in a dynamic equilibrium with so-called wild type HEV which do produce normal capsids. Therefore, the DI viruses are parasites upon the wild type population of HEV, using their capsids to package the mutated RNA for movement to the next cell. Using a mouse model of CVB3-induced myocarditis, in which viral RNA was detectable in the heart tissue for many days after cytopathic virus was no longer detectable in cell culture, we searched for evidence of DI forms of CVB3 RNA but were repeatedly unsuccessful.

We decided to examine the entire viral RNA genome that was present in these mouse heart samples, asking the basic question: are there deletions anywhere else that might explain this odd phenomenon? When this was done, we discovered that one of the ends of the single strand of RNA that makes up the viral genome, was missing: these viral genomes were then called 'terminally deleted' or TD(8, 18, 19). What makes this discovery fascinating to virologists, is that the sequence which the virus naturally deletes, was hitherto thought to be absolutely essential for virus replication. Our results, however, showed that while this sequence was very important for efficient CVB replication, it could nonetheless be done away with, and yet have the virus survive.

The cost of this survival is, however, extremely slow replication. A further cost is that this survival can occur only in cell populations that do not divide anymore or divide very infrequently as in muscle tissue. It is this reason why we were able to find these novel virus populations in heart muscle

of experimentally inoculated mice(19) and later, in human heart(8). There are some cell cultures that do not divide continually but stop dividing when the cells contact each other; only in such cultures can CVB-TD populations occur(18). This is very different than current cell culture models for enterovirus infections in which most aspects of the viral biology are examined in immortal continuously replicating cells. While this is a good model for the short term infection of the gastrointestinal tract in which the virus infects, rapidly produces progeny virus and is excreted to infect another individual before the immune response can curtail infection, much of the pathology associated with enterovirus infections is in other differentiated tissues in which relatively little cell turnover may occur. In these non-replicating (or only intermittently replicating) cells, the wild type virus is at a disadvantage because these cells lack key cytoplasmic factors essential for rapid replication. However, the low level replication of the TD viruses is favored in these cells and as the intracellular portion of the virus replication cycle is much longer, it is relatively hidden to the immune system. Much of our current research focus is upon the mechanism of selection of the TD populations in such cell cultures or tissues.

These results provided an answer to the conundrum of failing to find cytopathic virus in myocarditic heart samples despite the ability to find viral RNA. Indeed, virus (in TD form) does exist in such samples but because the TD populations replicate so slowly and produce so little virus, they are difficult to detect. However, because the defect is not in a part of the viral genome that makes viral proteins, they do make all the viral proteins and even virus particles. But what does the finding of TD genomes mean for HEV disease?

Chronic disease associated with HEV infections

The previous discussion has demonstrated that HEV can persist for longer periods of time in the immunologically-normal host

Human enteroviruses and chronic infectious disease *(continued)*

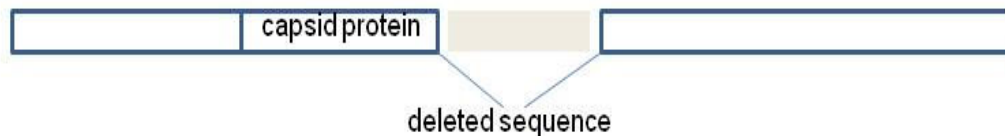
Figure 2. Depictions of enteroviral genomes that have been characterized and can persist for long periods of time in the infected cell. The DI genome (panel A) deletes a portion of the capsid protein coding regions, while the TD genome (panel B) deletes from the end of the genome in a non-translated region (produces no protein but is involved in viral RNA replication). Only the TD genome (panel B) has been shown to exist as a naturally-occurring event in humans.

(A) Defective interfering (DI) HEV genome

wildtype virus genome - replicates normally

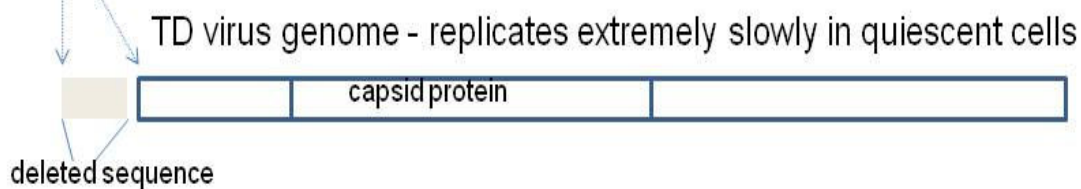


DI virus genome - defective replication needs wildtype to survive



(B) Terminally deleted (TD) HEV genome

wildtype virus genome - replicates normally



than ever had been suspected but that this came at a price to the virus: very slow replication and relatively very few infectious particles produced. In cases of chronic inflammatory heart disease (chronic myocarditis) or what is often thought to be a sequela of this condition, called dilated cardiomyopathy (DCM), HEV RNA has been detected in the apparent absence of cytopathic virus(4, 7, 21). We can now say with some certainty that in such cases, HEV-TD populations were present. In DCM, the heart is failing due to damage to the

cardiomyocytes (muscle cells of the heart). Others have shown that a HEV enzyme that works on and reduces proteins, called a protease, can damage an important cardiomyocyte protein called dystrophin(3) and that in a mouse model of this disease(33), dystrophin is cleaved despite the inability of the virus to produce infectious particles and this leads to DCM in the mouse, a scenario that is closely similar to the low level production of virus particles by TD virus populations. Therefore, in this chronic HEV-induced

Human enteroviruses and chronic infectious disease (continued)

disease, the long-term persistence of a slowly replicating HEV can lead to cell damage, due to the virus' own enzymes it uses to replicate, and this damage eventually impacts the function of the organ (the heart) itself.

Another chronic disease that is closely linked to HEV infections is type 1 (insulin dependent) diabetes (or T1D)(15, 30). Type 1 diabetes occurs due to an inability to control glucose metabolism which is an outcome from the loss of insulin-producing beta cells in the pancreatic Islets of Langerhans(17). Although some cases are thought to be due only to a specific expression of individual genetic traits, most T1D cases cannot be so easily explained and therefore, environmental factors (like infections) have been sought to explain how T1D is initiated(1, 20). One environmental factor that is high on any list, are the HEV: many clinical observations and experimental studies implicate HEV as agents that can and do trigger T1D onset in humans(15, 30). While CVB have been associated with T1D cases, other non-CVB HEV have also been implicated in T1D onset, further adding to the evidence for a role of HEV in T1D onset. At present, it is unclear whether the HEV involved persists in the host after the initial infection that sets the disease in motion, or whether it is more of a classical HEV acute infection, one that is rapidly cleared by the immune response. What is very clear, however, is that CVB can rapidly trigger T1D onset in a T1D-prone mouse called the NOD mouse if the mouse is already prediabetic from its own autoimmune attack on its pancreatic islets(14). This means that under certain circumstances (when one has autoimmune insulinitis present, and one is infected with an HEV against which one has no pre-existing protective immunity, and it is the correct HEV at the right dose), T1D in humans could likely be initiated by an HEV infection. Using the rapid onset model in mice to make inferences for humans, we would predict an HEV infection that rapidly kills enough beta cells will initiate T1D. However, the virus infection might not accomplish this: the virus might instead kill insufficient numbers of beta

cells for T1D to ensue. What then? This is where the autoimmune (in which one's immune system attacks oneself) aspect of T1D sets this disease apart from the previously discussed chronic heart disease. In T1D, enough insulin-producing beta cells must be destroyed in order for T1D to occur: this can happen by autoimmune processes, by virus attack, or both occurring together. We are currently assessing whether long-term persistence of HEV is a factor in both the NOD mouse model of T1D and in human beings.

Chronic fatigue syndrome and the link to HEV infection

In a paper that received much notice, Chia and Chia showed that HEV RNA and protein were detectable in the great majority of stomach biopsy tissue samples from patients diagnosed with chronic fatigue syndrome (CFS) but only in few biopsy samples from control patients without the disease(9). This report has suggested that a commonly circulating human virus group might be a primary etiologic agent involved in CFS, a disease that is marked by a difficult diagnosis and a near complete lack of understanding about what agent(s)/mechanism(s) trigger the disease.

As we have seen from the previous discussion, HEV may be able to initiate a disease process just from an acute infection, which is then resolved, or from a continuing infection as well, involving a persistent virus population. Persistence is, however, a relative term. In an immunologically-normal individual, *i.e.*, one who is able to mount normal vigorous immune responses against infectious agents, an HEV infection may be able to persist via a TD genome mechanism for some weeks, perhaps months, but eventually will be eradicated by the immune response. Thus, such infections are temporary (unlike herpesviruses or HIV). Although HEV are common viruses, the very high positive correlation with the CFS stomach samples was surprising. In other known associations of HEV with human

Human enteroviruses and chronic infectious disease (continued)

diseases, such high correlations have not been observed. Poliovirus caused paralytic disease during epidemics(22) but only about 1 out of every 100-200 infections involved life-threatening paralysis. The HEV, thought to be primarily CVB, which have been closely linked to causing myocarditis, have been detected in about 15-20% of samples in a variety of studies(21).

To explain the high number of positive stomach samples with CFS, one must consider the possibility of a continuing process in CFS patients of new infections with different HEV serotypes and/or a significant number of persistent infections in the stomach. The difficulty these workers had in culturing the viruses from stomach tissue, would be consistent with either HEV strains that do not replicate well in standard tissue culture systems and/or the viruses exist in a form that is difficult to detect. While most HEV do replicate in certain cell cultures, others require the use of suckling mice(27). It is interesting to consider that a HEV-TD population would fit such a description of a 'difficult to culture virus'.

At present, these findings are highly intriguing but need also to be considered with the proverbial 'grain of salt'. It is of the highest and immediate importance to identify the HEV in these stomach biopsies in order to verify and move forward the theory that HEV are involved in the CFS etiology. Are they a specific serotype of HEV or are they many different types?

This can be determined without culturing the viruses, by amplification of specific genome regions and determination of the RNA sequence(5, 24-26). Once established which specific HEV are present, relevant model systems might be developed using cell cultures and possibly mice, to study the CFS disease onset process.

Summary

Basic research into the biology of the HEV has lead to truly fantastic discoveries which

in turn, have lead to 'bench to bedside' advances. Understanding how to culture animal cells in the laboratory, made possible propagation of the agent that causes polio and subsequent studies in primates, work that in turn lead to the development of the successful poliovirus vaccines from which we have all profited. A search for other viral agents that induce polio-like disease lead to the discovery of the coxsackieviruses and indeed many other HEV.

The development of a mouse to study retinal disease produced the NOD mouse, a highly useful mouse strain that is regularly used in studies of T1D. We know that serendipity and planning go hand in hand and often in the laboratory, are hard to tell where one begins and the other leaves off.

As scientists who focus on all things enteroviral, we are especially interested in the findings of Chia and Chia that suggest the potential for an HEV link in CFS etiology.

Our finding that a deletion in the terminal portion of the CVB genome, was the mechanism by which HEV can persist, could not have been predicted based on what was known. This finding has opened a completely new and quite unsuspected chapter in the very well thumbbed volume on enterovirus biology.

This was elegantly enunciated by Louis Pasteur in his famous quotation: "Where observation is concerned, chance favors the prepared mind." Without the existence of basic science, most of what we know take for granted in medicine would not exist.

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.

Human enteroviruses and chronic infectious disease (continued)
Acknowledgements.

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We also sincerely thank a group of concerned individuals who have lost family due to enteroviral heart disease, for their generous support.

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

More details at -
www.enterovirusfoundation.org

SEVERE ME – A NORWEGIAN EXPERIENCE

Harald and Kjersti Krisner



The Krisner family from Norway whom we introduced on the Conference 2006 DVD in a TV programme (available from the Invest in ME web site) and in a follow up article has since experienced considerable changes.

Katrine, who has been ill since 1999, has become miraculously better in the past year. In 2003 she woke up from a coma like condition only to become seriously ill again in 2006. At that time she was left bedbound for 2 more years in total darkness, being tube fed and without any ability to communicate at all.

Her condition was plagued with severe symptoms, and we fought to keep her alive. In December 2007 she was prescribed broad spectrum antibiotics due to an infection. After 2 ½ months on this medication, she suddenly responded in February last year.

She started to speak slowly.

Light and sound sensitivities became a little bit better also.

She told afterwards how she had gradually felt getting better, but had no means of communicating it.

After further blood tests we carried on with the treatment, but now with three different antibiotics at the same time. After two more months, at times with debilitating side effects,

The Krisner Family and ME in Norway

In 2006 we were introduced to the Krisner family from Norway whose three children were severely ill with ME.

All three siblings Frode, Katrine and Bjørnar lived normal lives before their sickness. Bjørnar was a journalist and TV presenter.

In 2006 they agreed to appear on a Norwegian TV programme to highlight the plight of severely ill ME patients.

Doctors could not explain why all three siblings had the illness. They did not know whether it was genetic or if there were other factors which forced three young people to live several years in the darkness and confined to bed.

At the time of the program the three siblings were 29, 26 and 20 years old. Frode became sick when he was 7 years old, Katrine when she was 20 and Bjørnar became really sick when he was 26.

No one could predict if the siblings would ever get better nor say what can be done to return them to a normal life.



everything moved forward quickly, and on the 10th of May 2008 she was in the sitting room for the first time in two years.

A couple of weeks later she could venture out into the garden for the first time in seven years. At this point she was able to be without sunglasses indoors, but outside sunglasses were still needed.

The improvement this time is completely different from the one in 2003-2006. It is so in every aspect.

The change in May was enormous, almost miraculous.

We saw the illness losing its hold, whilst with the previous period of improvement it was a constant battle against something overpowering.

Since June last year Katrine has been a patient of Professor Kenny De Meirleir.

One tries to remove causes successively and build up the immune system. The treatment, change of seasons, infections, continuing illness and other things, cause the condition to fluctuate.

She has since May 10th last year, been up every day and this is something of an experience for us around her.

She is engaging, reflectful, caring with lots to give and convey, hungry for information and knowledge, is realistic in relation to the illness and at the same time plans for the future.

She still has to be careful and take it easy.

Experience tells us, also this time, that going too fast brings relapses or, at the very least, slower recovery.

Her younger brother, Frode, who is 23 years old and has been ill since he was 7, also experienced great improvement last year after several months on a similar treatment protocol as Katrine.

He had an experience of living with an 'abundance of energy' for the first time which was a fantastic experience for him.

To be free from looking for a chair to sit down on, to avoid detailed planning and giving up a lot the following days if he was out with friends the evening before, to be able to live more like everybody else on good days, became a

great experience.

The previous summer was a summer when he could do more and he and his best friend, who has been fantastically supportive all these years, went to south of France for a holiday. Being such car enthusiasts, they could both experience many things they had dreamt of in the past years.

Frode has gradually built up his IT company. He still has to live a restricted life, but he has a far greater capacity than before.

Bjørnar, the eldest in the family, now 32 years old, was the one who was the main character in the 2006 film when he was interviewed in the dark.

The TV programme gave the severely ill a face and set in motion a lot of emotions and engagement.

The fact that he was a TV journalist with an exciting career and ended up as a patient needing care, made an impact on many of his colleagues. The effort of being on TV such as having a hair cut and shave, took a lot of energy out of him and led to further deterioration of which he still has not recovered.

At present Bjørnar can communicate with signs and speak a little if needed or when he has more energy. If he speaks more than his energy levels allow, it leads to increasing symptoms which in turn can be the start of long term worsening of his condition.

This balancing of trying to avoid worsening of the condition, is important in moving the condition in the right direction.

Last year in the spring he was put on a similar treatment as his siblings but there was no big breakthrough.

Four months ago it looked like his condition was finally on its way to improving. At that time his test samples that were sent to a specialist laboratory were found to be positive for an African amoeba. After a few days on a strong amoeba treatment protocol, he experienced a radical change in his abdominal pain, hunger and bowel movement function. He is still under treatment for many other things that were found. He feels he is getting gradually better.

SEVERE ME – A NORWEGIAN EXPERIENCE

All three siblings have since June last year been undergoing treatment under the guidance of Professor Kenny De Meirleir. He came along after the extra blood tests that led to treatment had been done. His findings fit in with those performed earlier.

It is fantastic to experience improvement and great to see two of our children come back to life. We hope that we shall experience Bjørnar coming out into daylight in a short while.
Life is exciting.

To be continued next year.

Harald and Kjersti Krisner, parents (May 2009)



Katrine (above) – a photograph taken on her 30th birthday in May 2009.

ME STORY

The following day the psychologist came to give me the results, his words were these:

"If you are to be believed, and your answers truthful, then you have the mental age of a senile 71 year old, and I should section you immediately!

Now if you would truthfully like to tell me what personal experience led to your M.E. then I might be able to help you! What devastating event led to this mental problem, what made you so depressed?"

I was appalled at this approach to my illness!! I told him in no uncertain terms that there had been no devastating event, that I had not been depressed, that actually my life for the previous couple of years had been remarkably uneventful but extremely happy.

He continued to insinuate that something must have happened and that I was obviously depressed - so I pointed out to him that the only event had been me becoming ill and that any depression I had was a result of that!

He then told me he would recommend that I be placed in another hospital to have further psychological review because I was obviously not trying and was actually deliberately acting ill to gain attention!

- Debbie

ME STORY

In 2004 I caught a kind of flu with an infection of the gut and I never recovered.
I needed 3 years for a diagnosis.

It was a infernal trip into the jungle of the German health care system.

At the onset there was a kind of outbreak in my workplace.

The whole staff had been affected by ME-symptoms.

In 2007 Prof. Dr. de Meirleir in Belgium attested me: This patient suffers from ME/CFS (WHO 93.3).

- Roland



Call to Action

Why I Support Invest in ME

Like a lot of people, I had no real knowledge about M.E (Myalgic Encephalomyelitis). I just assumed it was some luxury illness or 'yuppie flu', because that is the way the media, especially newspapers had portrayed this disease. Then my sister Sophia developed severe M.E. and two years into her suffering, it began to dawn on me that perhaps I had grossly underestimated M.E.

I support Invest in M.E. because they understand the true nature of M.E and help many sufferers of this disease.
It was partly ignorance that killed my sister.

Yes you read that right, Sophia died from M.E.

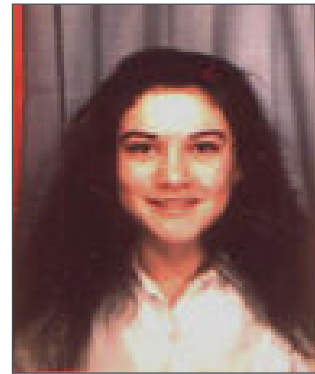
She was 32 and her suffering and death were largely preventable. Sophia's last wish was to help others not go through what she did.

My sister was disbelieved by her doctors about the true physical nature of her illness. She was accused of attention seeking and having 'unresolved issues' and she was treated as if her illness had its roots in her mental health.

My mum who was my sister's main carer was accused of enabling Sophia's illness for the simple crime of *believing* that her daughter was *physically* very ill. One of Sophia's doctors actually wanted to section my mum. I wish I were exaggerating but proof of all this is on SophiandMe.org.uk.

Invest in ME is a charity that understands that M.E is a physical disease and that M.E has been categorised as a physical neurological disease by the World Health Organisation since 1969. The way M.E. is treated in this country is contrary to how a physical, neurological disease should be treated. In the UK, psychiatrists took charge of the care of people with M.E., but this disease is not a mental illness. It is like being treated by a dentist for a broken leg. The wrong people are in charge of a disease that they have no expertise in dealing with.

Sophia Mirza



Roisin Mirza is the sister of Sophia Mirza and is a qualified nurse.

Sophia died from ME. Disbelieved by those providing healthcare for her condition, she was sectioned by psychiatrists who neither understood her condition nor seemingly cared to analyse her symptoms in a medical way. Sophia was "sectioned as a result of exercising her right not to go into a particular ME Clinic.

Despite the fact that she was bed-bound, she reported that she did not receive even basic nursing care, where her temperature, pulse and blood pressure, were never taken. Sophia told me that her bed was never made, that she was never washed, her pressure areas were never attended to and her room and bathroom were not cleaned. From Tuesday 22nd November, Sophia could not move an inch, neither could she sleep.

On Friday 25th she died.."

- taken from Sophia's story on the IiME web site

Call to Action - Why I Support Invest in ME

(continued)

We don't know how you get/develop/contract M.E, and we don't know how to cure it and therefore we could all be at risk from M.E.

So why are psychiatrists and the mental health sector given free reign over M.E? The simple answer is 'kerching' and politics/power play. There is a lot of money at stake for the treatment and research of this disease. It is in certain group's interests to keep M.E treated as a mental illness. The Government is advised by psychiatrists about the treatment of the disease of M.E and it is in their interest to advocate mental health treatments.

It is also in medical insurance companies' financial interests to keep M.E treated as a mental illness. If M.E funding were to go to the physical health camp, it would have to battle with the big boys such as Cancer and Heart Disease for funding. In the mental health camp there is far less competition.

The ring of 'kerching' is louder than the cry of truth at the moment. However the truth will out, and the sooner M.E is seen and treated as a physical illness the better for everyone. This is not just better for M.E patients and their carers, it is better for everyone. The false security of M.E getting labelled as something in mental health is a dangerous myth. You cannot catch a mental health disease, but you can catch/develop a physical disease.

Multiple Sclerosis and Parkinson's disease were considered mental illnesses before they were wrestled out of mental health and put in their rightful place in physical health treatment. M.E is not the first and will probably not be the last disease to be wrongly taken by the mental health sector.

By supporting Invest in ME you are helping liberate everyone. This (event) happened to Sophia but it could happen to anyone of us. My sister was condemned as mentally ill and referred to a psychiatrist, even though no mental health checks were done and it was

blatantly obvious to anyone that Sophia was severely physically ill.

Sophia refused treatment at an ME clinic where they treat ME patients with methods such as GET (Graded Exercise) and CBT (Cognitive Behaviour Therapy). These treatments have been proven to make M.E patients WORSE. The clinics' own statistics state that Graded Exercise makes people with severe ME worse. Sophia was given a 'get well by a certain date or be sectioned' ultimatum which she failed to get well for.

Sophia refused to go to the clinic because she was just too ill to be able to risk treatments which would probably cause her great harm. This was a sane decision by Sophia. As a result of making a sane decision an insane one was taken by her doctors. Sophia was sectioned into a mental health hospital and she never recovered from this experience.

Sophia's could not tolerate light, noise, movement or smells. She lived the last few years of her life in the dark, in bed and couldn't even read a book or listen to music. She was in constant pain and if this were not bad enough, she had to live under a blanket of fear and was treated as if she were mentally ill, despite overwhelming evidence to the contrary.

My sister's post-mortem revealed the physical evidence of M.E in her spinal column. It is a shocking disgrace that Sophia had to die to be believed.

I trained as a nurse through my sister's illness and I saw how M.E was viewed from the other side. I never confided in anyone during my nurse training and nurse working time about my sister having M.E, because of the stigma attached to this disease. I didn't risk confiding in people because when I had tried confiding in people before, I was met with plastic psychiatry about 'perhaps she has unresolved issues'.

If you got M.E from having 'issues' the whole country would be down with it. There was also the risk that a well meaning but ignorant person would add fuel to the fire and go to the

Call to Action - Why I Support Invest in ME

(continued)

authorities with their 'concerns'. This practise is encouraged by psychiatrists who use peoples 'concerns' to back up their mental health treatment assault.

By supporting Invest in ME you are supporting human rights. Sophia was stripped of her human rights because of the mental health label. By supporting and bringing to light the truth about the disease of M.E you are helping to save lives. You are helping prevent another Sophia story happening.

By supporting Invest in ME you are saying that M.E is a physical disease that needs to be treated as such. This matters to those countless M.E sufferers and their carers that you understand they are genuinely physically ill. There is no physical diagnostic test for ME at the moment but how can there be a physical marker test for ME if no research money is put there?
This must change.

I will be going back to my old nursing school and giving a talk about Sophia and her ME on June 8th.
Ignorance of ME is producing much unnecessary suffering.

We need as much help as possible to turn the image of M.E around.

Racism is rightly taken very seriously, but what about 'diseasism' ? There is a stigma with M.E that is similar to a sixteenth century witch hunt. The accusation of being called mentally ill, is similar to that of calling a woman a witch. Treating someone as if they are mentally ill, does not make that person mentally ill. How can someone prove they are physically ill if the doctors treating them do not believe their own eyes and ears?

Even without a diagnostic test for M.E there are still physical abnormalities that would show up in a blood test and other basic health checks. Many doctors are reluctant to physically test for ME because the "experts' " advice that it 'encourages aberrant illness beliefs'.
ME is not a belief, it is a fact.

ME is as much a 'belief' as I 'believe' in gravity and those psychiatrists 'believe' they are medically trained.

We need research into the physical nature of M.E. We need people to be as aware of M.E as they are of cancer.
You wouldn't accuse a cancer patient of imagining their illness because they had unresolved issues.

Not many things in life are black and white, but this is.

There is no 'confusion /controversy' about the disease of ME except the confusion the 'expert' psychiatrists have put there. By muddying the waters , these psychiatrists, many of whom are in the pockets of medical insurance companies, are keeping M.E in their domain. Chronic Fatigue Syndrome (CFS) and M.E are being lumped together as the same disease but they are not the same. M.E. is a physical neurological disease, and CFS is am umbrella term for any disease with fatigue in.

Chronic Fatigue is classified by W.H.O as a mental health illness, but M.E is classified as a physical, neurological disease.
One can see how the lack of clarity starts to happen.

A small powerful band of psychiatrists have, for years, clouded and complicated the understanding of the disease of M.E, not just in the consciousness of ordinary people, but in the minds of doctors, psychiatrists and the Government, by talking about ME and fatiguing syndromes in the same breath.

People are still suffering unnecessarily from the physical disease of ME and from the unspoken accusation that it is 'all in their mind' because of a small group of doctors' greed for money and position. People are living under fear of being sectioned because they 'believe' they are physically ill with M.E. Carers of those with ME have a much higher rate of being accused of Munchhausen's By Proxy .

Call to Action - Why I Support Invest in ME

(continued)

It is scandalous that the very vulnerable ME patients are not only not helped, but actually *discriminated* against because they have M.E.

Please help us change this.

Anyone can get M.E. Sophia was half Pakistani and half Irish. This is not just a white person's disease. We are all at risk and we need urgent research and treatment into the physical nature of this disease.

Behind the closed doors of courts, children are being torn away from their parents. These parents are silenced by these same courts.

Tell the mental health sector to 'Get your hands off M.E' and put M.E back in its rightful place, back where it belongs, back to where the W.H.O. put it in 1969, back in the field of physical disease.

ME STORY

I now live on DLA and have to use a wheelchair. I spent years being told I had depression, I was attention-seeking, difficult, lazy.

I tired too hard to do the things other children/ young adults did and failed. I felt hopeless and helpless many times.

However I refused to give up fighting. THREE years ago after another round of arguing with doctors and neurologists and being told by a neuro psyche I was not genuinely ill my GP found missing notes from the 1980s - notes that had been missing for over 20 years.

There in black and white were handwritten notes than indeed I had attended the doctors who had noted possible encephalitis.

- Lynn

ME FACTS

In 2003, Byron Hyde, medical adviser on ME/CFS to the Canadian Government, pointed out that

"ME in adults is associated with measurable changes in the central nervous system and autonomic function and injury to the cardiovascular, endocrine and other organs and systems.

The patient with the diagnosis of ME/CFS is chronically and potentially seriously ill.

These ME/CFS patients require a total investigation

and essentially a total body mapping to understand the pathophysiology of their illness and to discover what other physicians may have missed.

A patient with ME is a patient whose primary disease is central nervous system change, and this is measurable.

The belief that ME/CFS is a psychological illness is the error of our time".

(The Complexities of Diagnosis. Byron Hyde. In: Handbook of Chronic Fatigue

ME STORY

I have been diagnosed with CFS they (the NHS) will not have ME in their vocabulary.

Everything is a fight, to be heard, to be listened to, just to be BELIEVED.

I wish with all my heart that I just was a bit tired like people think, I would chop off my arms to be just tired. My life is a process of trying to get through the day and perhaps I'll have a day where I'm

not so bad

- Maxine

DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY

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ABSTRACT

Often Chronic Fatigue Syndrome (CFS) patients have weight issues, and weight reduction regimens can increase fatigue. Therefore, we initiated a weight loss clinical trial using an all natural oral supplement mixture containing an FDA-approved amylase inhibitor plus NTFactor™, which is known to safely reduce fatigue in aged subjects,¹ chronic fatigue² and CFS.³ The objective was to see if subjects could safely lose weight without increasing appetite and fatigue and without changing eating or exercise patterns or using drugs, herbs or caffeine. A 2-month open label clinical trial was initiated with 30 patients who used an oral mixture (Healthy Curb™) of amylase inhibitor (500 mg white kidney bean extract) plus 500 mg of NTFactor™ 30 min before each meal. Weight and measurements were taken weekly, appetite was assessed⁴ and fatigue was determined using the Piper Fatigue Scale.⁵ Sixty-three percent of the participants lost an average of 6 pounds along with 2.5 and 1.5 inch reductions in waist and hip circumference, respectively, and the entire group of participants lost an average of 3 pounds with average reductions of 1.5 and 1 inch waist and hip circumference, respectively. Participants experienced gradual and consistent weight loss along with waist and hip, body mass index (BMI) and basal metabolic rate (BMR) reductions during the entire trial. There was a 44% reduction in overall hunger with reduced cravings for sweets; therefore, notable appetite suppression occurred. Using the Piper Fatigue Scale the entire test group showed an average of 23% decrease in overall fatigue. Blood lipid profiles generally improved, suggesting improved cardiovascular health, and no adverse effects were noted clinically or found in blood chemistries.

Conclusions: The vast majority of the subjects in this trial lost weight, showed decreased waist and hip measurements and overall body mass. Their overall fatigue was reduced, and they experienced marked appetite suppression. The product was completely safe and void of any side effects and was extremely



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ME RESEARCH

"Many studies have found that the immune system appears to be in a state of chronic activation (and) genes that control the activation of the immune system are abnormally expressed in patients with this illness. A number of studies have shown that there probably are abnormalities of energy metabolism in patients with this illness".

**Professor Anthony Komaroff of the
Harvard Medical School**

DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY

(continued)

well tolerated. HealthyCurb appears to be a safe and effective means for CFS patients to manage weight without changes in eating or exercise patterns.

INTRODUCTION

Being overweight or obese can present health issues and may also lead to serious chronic illnesses. Dieting is difficult because dieters are unable to endure the commitment required to achieve their weight loss goals. One of the most common complaints of dieters is the constant feeling of hunger associated with reducing calorie intake. Another complaint dieters experience is the lack of energy due to decreased caloric consumption. Nutritional Therapeutic, Inc. has developed a safe, all-natural food-based supplement (Healthy Curb™) that has been reported to reduce appetite, increase energy levels, reduce fatigue, block starch uptake and help with weight management. The supplement contains NTFactor™, which has been shown to reduce fatigue and repair mitochondrial membranes.^{2,3} This study was designed to explore the degree of appetite suppression, the degree of energy level, fatigue reduction, changes in specific blood markers for metabolic health and the amount of weight loss and reduction in waist and hip measurements in a 60 day trial.

PROCEDURES

A two-month open label clinical trial was initiated with 30 patients, ages 18 and older, who used an all-natural oral mixture (Healthy Curb™, <http://www.healthycurb.com>) of FDA-approved amylase inhibitor (2 tablets containing 500 mg white kidney bean extract plus 500 mg of NTFactor™) 30 min before each meal. All subjects filled out a medical intake form at Tustin Longevity Center. The medical staff determined if participants were qualified to enter the study based on medical history. Chronic fatigue was an important entry criteria. Weight, waist and hip measurements were taken weekly, appetite was assessed by the procedures of Arumugam et al.,⁴ and fatigue

was determined using the Piper Fatigue Scale.⁵

Blood samples were taken at the beginning of the study and at the end of the study. Weight, body composition and measurements were taken every two weeks until the end of the study.

During this two-month study the NIH guidelines for alcohol consumption were followed: "Moderate drinking is one drink a day for women or anyone over 65, and two drinks a day for men under 65."

RESULTS

Weight and Girth Reduction: The entire group of participants lost an average of 3 pounds (Fig. 1a) with average reductions of 1.5 and 1 inches in hip and waist circumference, respectively (Figs. 2a, 3a). Sixty-three percent of the participants (responder group) lost an average of 6 pounds (Fig. 1b) along with 2.5 and 1.5 inches reduction in hip and waist circumference, respectively (Figs. 2b, 3b), and participants experienced gradual and consistent weight loss along with waist and hip reductions during the entire trial.

ME STORY

I had suffered neurological symptoms for a number of years but by 2003 they had reached the point where I couldn't ignore them any longer.

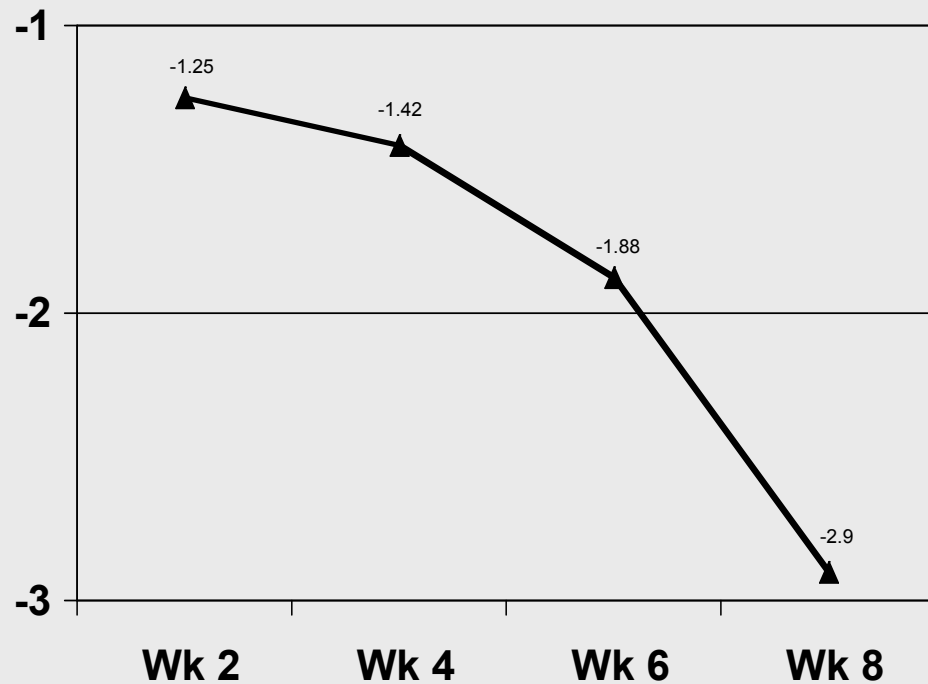
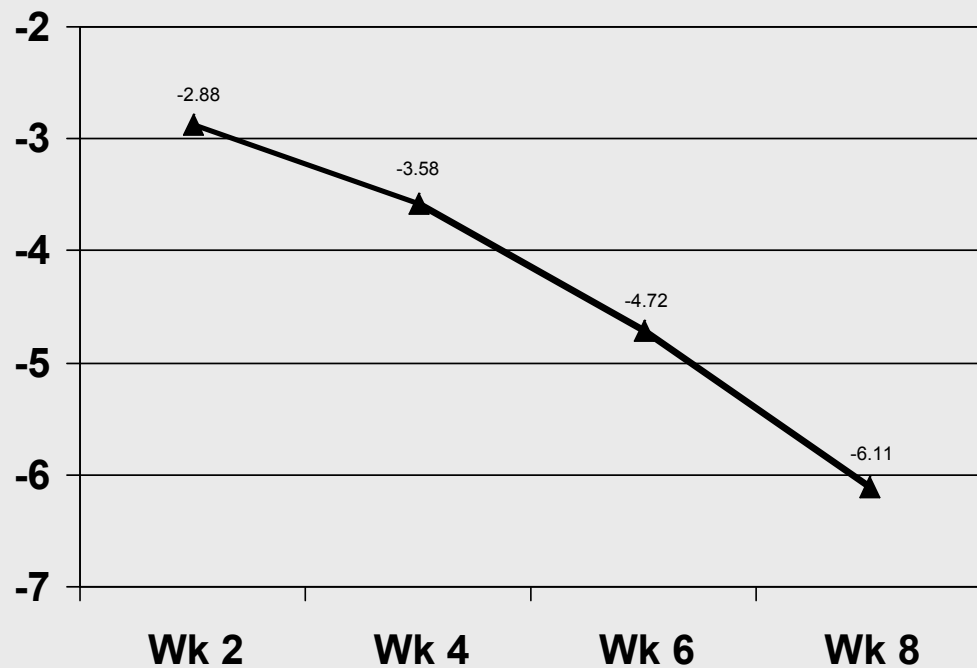
I decided to go to the doctor. By great good fortune I took the first appointment available and saw a GP new to the practice.

I told her my story, we discussed ME and she said she neither believed nor disbelieved in the illness.

She was more interested in the patient than a 'tag', she said.

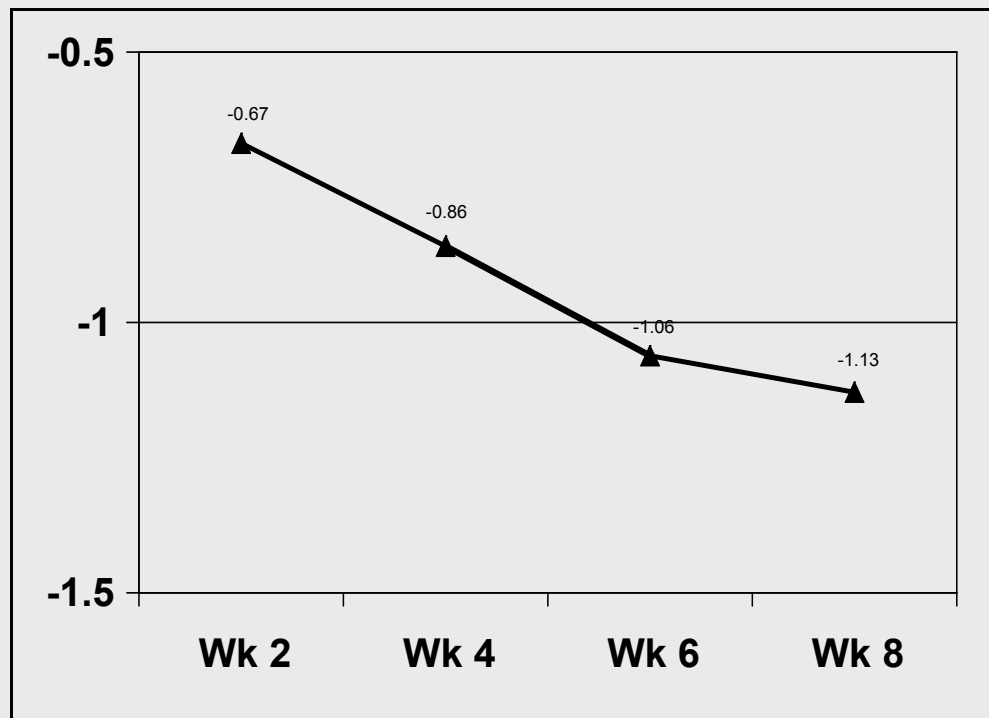
But for the first time since my diagnosis I had found a doctor who actually listened to me.

- Jim

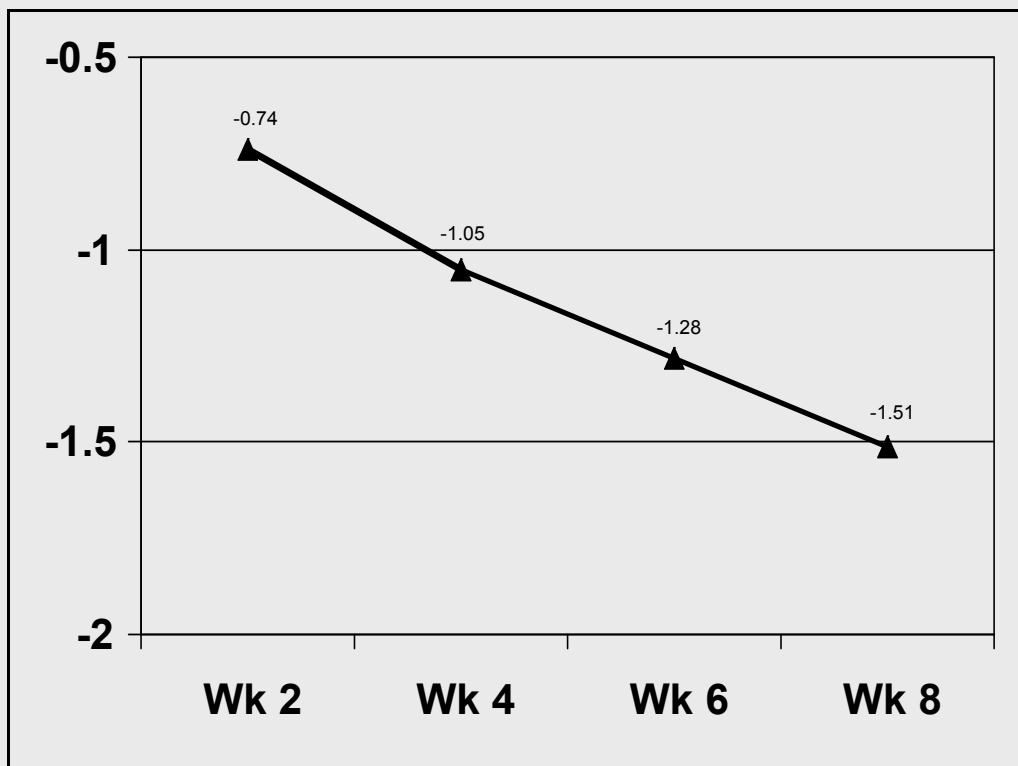
DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY*(continued)***Figure 1a****Average Weight Loss (lbs) Entire Group****Figure 1b****Average Weight Loss (lbs) Responder Group**

DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY*(continued)***Figure 2a**

Average
Hip
Measure
Loss
(inches)
Entire
Group

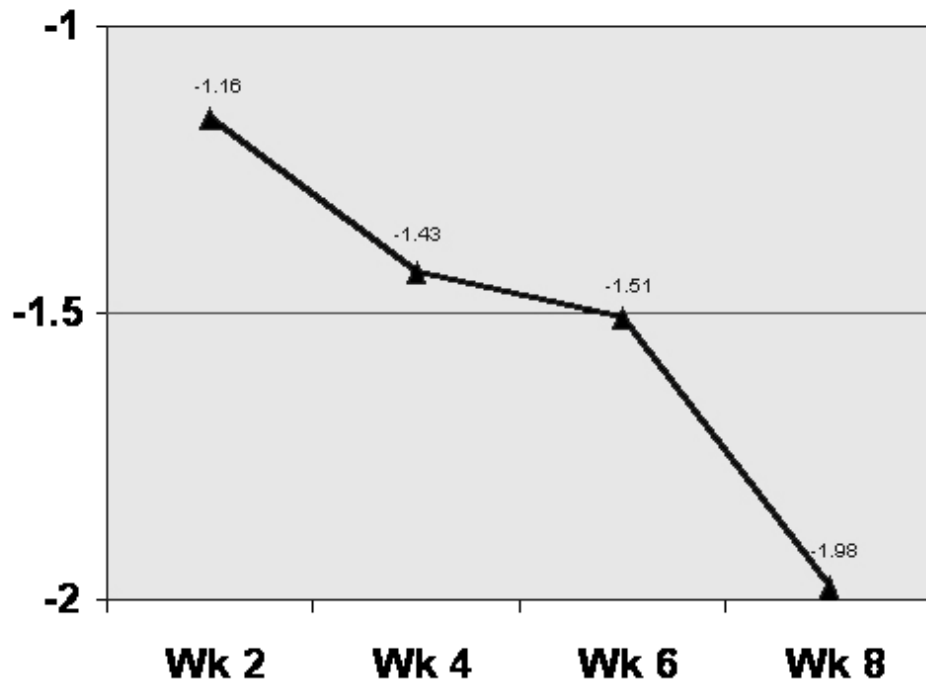
**Figure 2b**

Average
Hip
Measure
Loss
(inches)
Responder
Group

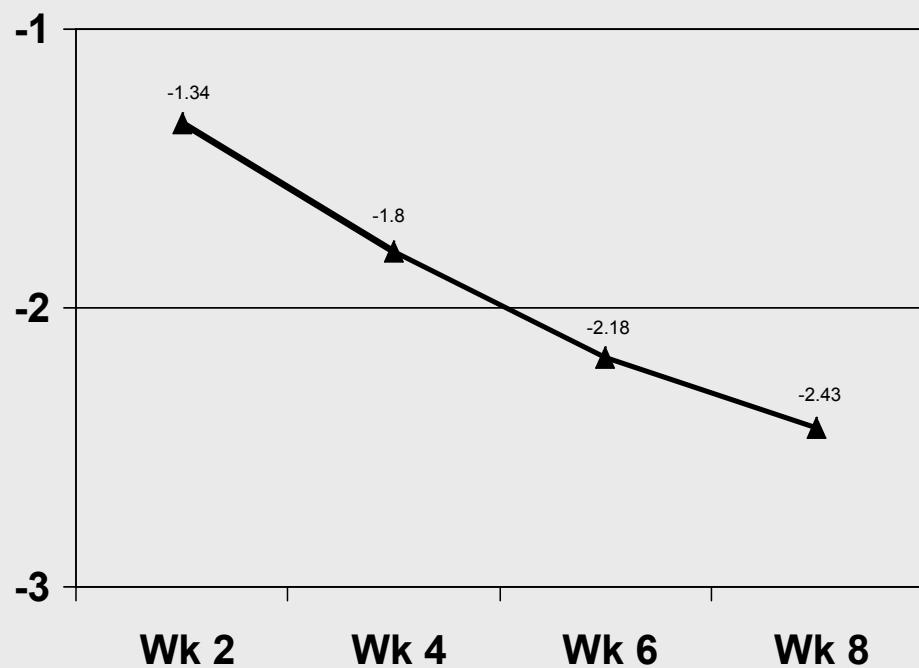


DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY*(continued)***Figure 3a**

Average
Waist
Measure
Loss
(inches)
Entire
Group

**Figure 3b**

Average
Waist
Measure Loss
(inches)
Responder
Group

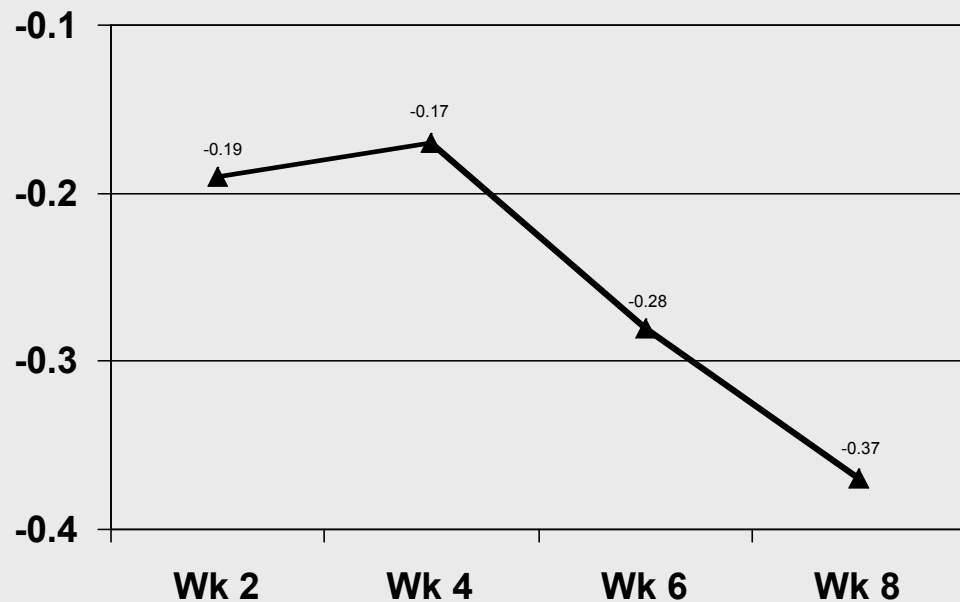


DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY**(continued)**

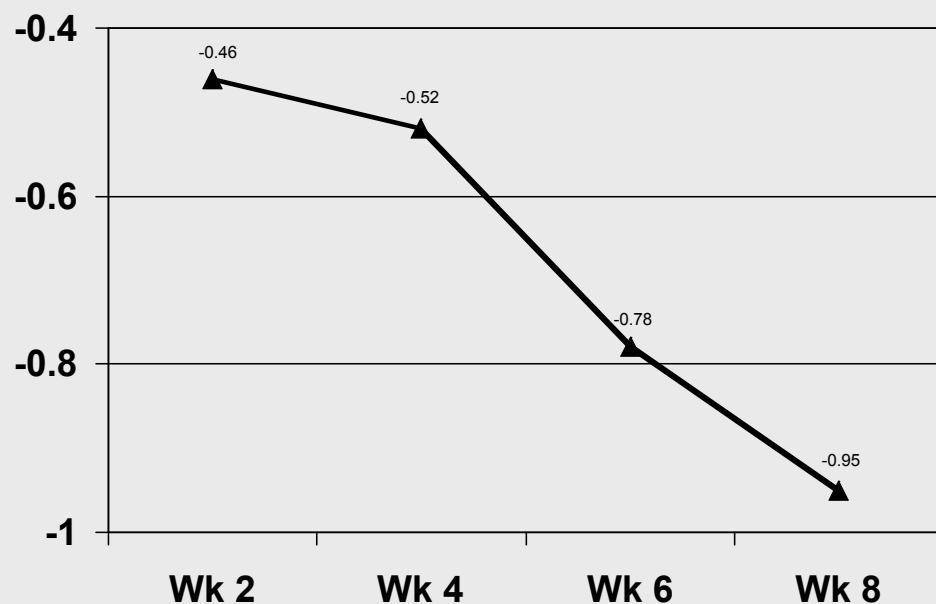
Body Mass Index Reduction: Body mass index (BMI) was calculated as the weight (in pounds) times 703 divided by height (inches) squared. There was a reduction in average BMI in the entire group of 0.18 (Fig. 4a) and in the responder group of 0.49 (Fig. 4b).

Figure 4a

Average
Body Mass
Index
Entire
Group

**Figure 4b**

Average
Body Mass
Index
Responder
Group



DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY*(continued)*

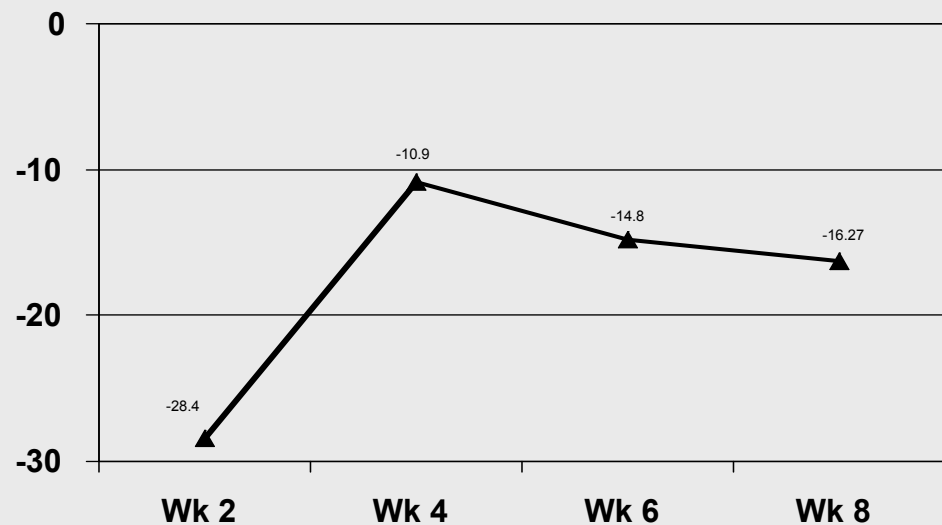
Basal Metabolic Rate Reduction: Basal Metabolic Rate (BMR) uses the variables of height, weight, age and gender to calculate a rate of resting metabolism. The overall change in BMR and change in the responder group are shown in Figs. 5a, 5b. These were calculated as follows:

Women: $BMR = 655 + (9.6 \times \text{weight in kilos}) + (1.8 \times \text{height in cm}) - (4.7 \times \text{age})$

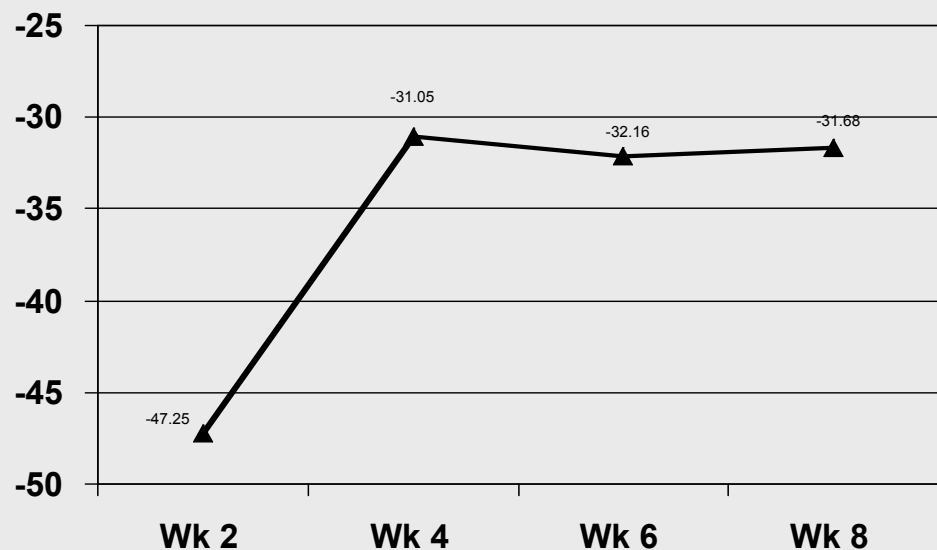
Men: $BMR = 66 + (13.7 \times \text{weight in kilos}) + (5 \times \text{height in cm}) - (6.8 \times \text{age in years})$

Figure 5a

Average
Basal
Metabolic
Rate
Entire
Group

**Figure 5b**

Average
Basal
Metabolic
Rate
Responder
Group

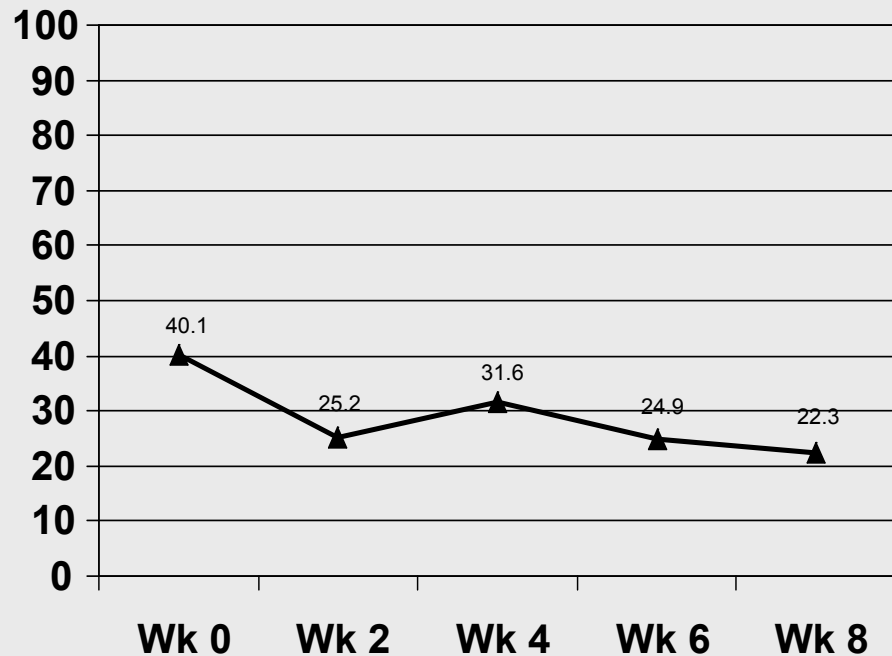


DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTfactor LIPID REPLACEMENT THERAPY*(continued)*

Appetite Suppression: There was a 44% reduction in overall hunger (Fig. 6) with reduced cravings for sweets; therefore, notable appetite suppression occurred.

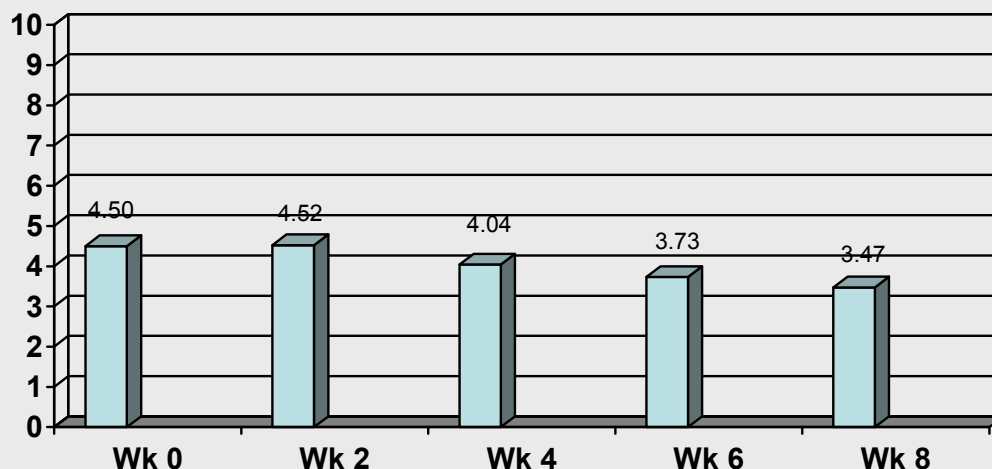
Figure 6

**Average
Hunger Index
Entire Group**



Fatigue Suppression: Using the Piper Fatigue Scale the entire test group showed an average of 23% decrease in overall fatigue during the trial (Fig. 7)

Figure 7. Overall Fatigue Scores



DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY

(continued)

Blood Lipid Profiles: Blood lipid profiles generally improved (Table 1), suggesting improved cardiovascular health, and no adverse effects were noted clinically or found in blood chemistries (data not shown).

Table 1. Blood Lipid Chemistry

Measurement	Day 0	Day 60
Glucose	104.8 mg/dl	104.4 mg/dl
Cholestrol	209.6 mg/dl	200.7 mg/dl
Triglycerides	142.6 mg/dl	129.2 mg/dl
HDL	56.9 mg/dl	58.0 mg/dl
LDL (Calc)	124.2 mg/dl	116.8 mg/dl
VLDL (Calc)	28.5 mg/dl	25.8 mg/dl
Cholesterol/HDL Ratio	3.9	3.7
LDL/HDL Ratio	2.4	2.1

DISCUSSION

Healthy Curb™ has proven to be a safe, all natural food-based supplement that allows weight control without the use of stimulants or herbs that could cause side effects. During the brief trial no adverse effects were reported, and blood chemistries and lipid analyses indicated that subjects actually had improved lipid profiles at the end of the trial. A common complaint while taking dietary supplements is the loss of energy and stamina.

Healthy Curb™ contains NTFactor™, a supplement known to naturally decrease fatigue and increase energy.¹⁻³ During the trial subjects reported increased energy and decreased fatigue, and this was shown by reduction in Piper Fatigue Scores. Thus a major problem in all natural weight loss products was overcome by including NTFactor™. They also had reduced hunger and reduced cravings for sweets.

DIETARY SUPPLEMENT HEALTHY CURB FOR REDUCING WEIGHT, GIRTH, BODY MASS, APPETITE AND FATIGUE WHILE IMPROVING BLOOD LIPID VALUES WITH NTFactor LIPID REPLACEMENT THERAPY

(continued)

Participants experienced gradual and consistent weight loss along with waist and hip, body mass index (BMI) and basal metabolic rate (BMR) reductions during the trial. Thus Healthy Curb™ proved to be a safe and effective weight loss supplement.

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Go to

www.investinme.org/IIMENewslettersubs.htm

NICE COMMENT

Commenting on the final Guideline, one GP from Bath said:

"The NICE Guidelines make it more difficult.

instead of separating ME from other illnesses with fatigue, NICE is just broadening the umbrella.

Now fatigue and sore throat is enough to have ME.

ME patients, and especially patients who don't have ME but

will be labelled as ME patients, will suffer as a consequence"

(Dr Andrew Ashley, eBMJ, 6th September 2007).

ME RESEARCH

A recent study found VP1, RNA and non-cytopathic viruses in the stomach biopsy specimens of CFS/ME patients with chronic abdominal complaints.

A significant subset of CFS/ME patients may have a chronic, disseminated, non-cytolytic form of enteroviral infection, which could be diagnosed by stomach biopsy.

For more information:

Chia, JKS, Chia, AY;(2008), "Chronic fatigue syndrome is associated with chronic enteroviral infection of the stomach," *Journal of Clinical Pathology* 2008;61:43-48.

From The Enterovirus Foundation - <http://www.enterovirusfoundation.org/associations.shtml>



The Current Situation in the U.S.

These are exciting times for patients in the United States.

The presidential election represented a significant shift in policy towards medicine, treatment, research, and the plight of the neglected.

In December, the Obama-Biden transition team asked for community meetings to discuss health care issues. A small group of us "met" online and produced a report on ME/CFS.

One community report from every state was chosen for the White House's new website for Health Reform – and ours represents my state of Delaware:

http://healthreform.gov/communityreports/delaware/delaware_19711.html.

It has already been read by Senators, Congressmen, and members of the executive branch.

The research group IACFS/ME met in Reno, Nevada, in March, with most sessions devoted to international biomedical research.

The new Whittemore-Peterson Institute in Reno is already bearing fruit using the tools of molecular medicine.

Dr. Nancy Klimas noted how exciting to see such diverse research presented in a cooperative, not competitive, fashion.

April 27, the U.S. CDC held a hasty stakeholders' meeting on their new 5-year plan for CFS and "fatiguing illnesses."

The Obama administration was, we believe, unprepared for the vehement response. Person after person testified to the consequences of having been rendered invisible by CDC's adoption of the name and concept of "chronic fatigue syndrome."

Mary M. Schweitzer, Ph.D.

Mary Schweitzer from Delaware, USA, was a tenured professor of history before being disabled with ME in 1994.

Mary has been an active and very passionate advocate for people with ME for several years writing articles and taking part in the CFSAC (Chronic Fatigue Syndrome Advisory Committee) meetings to allow the patient's voice being heard.

For four hours patients, advocates, and a few physician/researchers called for the immediate end of the current CDC program on CFS.

Consensus is building towards the goal of subgroups identified through objective biomedical testing, funding for treatment, and the establishment of Centers of Excellence as we have for cancer.

If CDC cannot help, then we want them to step out of the way.

Written comments on the CDC's 5-year plan can be sent from inside or outside the U.S. through June 30. See the website http://www.cdc.gov/cfs/meetings/2009_04.htm.

On May 27 and 28, the Chronic Fatigue Syndrome Advisory Committee (CFSAC) within Health and Human Services will hold its first meeting under the Obama administration. We are all hopeful that the entire approach to our disease will change, particularly regarding NIH and CDC.

Letter from America

The Current Situation in the U.S.

The agenda includes both the CDC's 5-year plan and the particular plight of children and adolescents with CFS.

Unfortunately, just as parents have had to fight to keep their sick children from being sectioned in the UK, in the U.S. we are seeing too many cases where a child has been forcibly removed from his/her parents and isolated in foster care.

Patients both at home and abroad are responding to the current plight of 16-year-old Ryan Baldwin, who has a CFS diagnosis. After being diagnosed with a related heart condition last year, Ryan qualified for social security payments for disabled children.

In January Ryan was suddenly taken away to a foster home. His parents were charged with "factitious illness by proxy" and denied access, even by phone.

Testimony from noted specialist Paul Cheney proved that the heart condition vacated a diagnosis of "factitious illness." The authorities then responded by asking the mother to plead to "dependency" [upon her child remaining ill].

She refused, and the court recessed for a month with Ryan still in foster care.

We are grateful for a letter sent to the governor of North Carolina by Invest in ME.

Anyone interested in helping with the case can find information here:
<http://cfsknowledgecenter.ning.com/profiles/blogs/free-ryan-baldwin>

The situation in the United States remains desperate for many patients, but there is also hope. If emphasis turns from the psycho-social to the biomedical, within five years diagnosable subsets can be identified and begin treatment.

We thank Invest in ME for its work in achieving that goal.

The European ME Alliance (EMEA)



Its aims are to -

- Establish correct recognition of myalgic encephalomyelitis as an organic illness requiring biomedical research to treat and cure
- Establish correct diagnosis of patients
- Establish specialised biomedical centres for education/treatment/cures

NICE COMMENT

For (NICE's Professor Peter) Littlejohns and his superiors to ignore completely how damaging this case (the Judicial Review of NICE guidelines of ME) has been to NICE is myopic in the extreme.

"The only thing worse than being blind is having sight but no vision." (Helen Keller)

How many more patients will need to challenge decisions by NICE before the government is forced to act and overhaul the management and the objectives of this organisation?

An organisation that purports to be "committed to promoting equality, eliminating unlawful discrimination, and actively considering the implications of its guidance for human rights" and yet is taken to court by the same patients for whom it claims to promote good healthcare – this is an organisation that deserves to be overhauled.

from –

<http://www.investinme.org/IIME%20Campaigning-NICE-Whats-Next.htm>

It was fourteen years ago, on 18th February 1993, that Dr Paul Cheney, Professor of Medicine at Capital University USA, Medical Director of the Cheney Clinic in North Carolina, and one of the world's leading exponents on ME/CFS, testified before the FDA Scientific Advisory Committee in a testimony that has become one of the most quoted in history:

"I have evaluated over 2,500 cases (of ME). At best, it is a prolonged post-viral syndrome with slow recovery.

At worst, it is a nightmare of increasing disability with both physical and neurocognitive components.

The worst cases have both an MS-like and an AIDS-like clinical appearance.

We have lost five cases in the last six months.

The most difficult thing to treat is the severe pain. Half have abnormal MRI scans. 80% have abnormal SPECT scans. 95% have abnormal cognitive-evoked EEG brain maps.

Most have abnormal neurological examination. 40% have impaired cutaneous skin test responses to multiple antigens. Most have evidence of T-cell activation. 80% have evidence of an up-regulated 2-5A antiviral pathway. 80% are unable to work or attend school. We admit regularly to hospital with an inability to care for self".

EPIDEMICS of ME

Epidemics of ME

**A Review of The Clinical Syndrome Variously Called Benign Myalgic Encephalomyelitis, Iceland Disease and Epidemic Neuromyasthenia by E D Acheson (American Journal of Medicine, 1959)
by Dr J Gordon Parish**

Many of the findings described in the landmark Acheson 1959 paper are very much relevant to our understanding of ME today. The disease was initially thought to resemble poliomyelitis until distinguishing features occurred; no patient developed the paralysis and muscle wasting seen in poliomyelitis which is a disease of the spinal cord.

Naldrett White, a Canadian neurologist, and Robert Burtch, an American family physician, described an epidemic in 1950 in Upper New York State in the USA in an area close to the Canadian border. They thought that muscles were directly involved during the initial infection. Accompanying a mildly elevated temperature to 99–100 °F (37.2–37.8 °C) in nearly every patient, there was pain and tenderness in various muscles sometimes with increased skin sensitivity over the affected areas making contact with clothes or bedding very unpleasant. In contrast to hypersensitivity, difficulty in moving limbs and numbness with diminished skin sensation on clinical testing suggested peripheral nerve involvement. Where there was weakness on using a hand and sensory symptoms, examination revealed an ulnar nerve disorder. Nerve roots were sometimes involved in the legs and were tender to pressure. This was associated with dragging of the legs on walking or foot drop. Another feature was lymphadenopathy in some patients. Enlarged tender anterior neck or axillary lymph glands are mentioned.

Examination of the blood and cerebrospinal fluid showed only minor abnormalities in two patients. White and Burtch thought that they might be dealing with an infection affecting

Epidemics are associated with ME.

From the Incline village episode to the Royal Free. Yet little is discussed about these. In the 4th International ME/CFS Conference Professor Harald Nyland will discuss the recent epidemic associated with Giardia in Norway. Yet this isn't new. It seems relevant to recall this review by Dr Gordon Parrish of an article by E D Acheson in the American Journal of Medicine

muscle. The standard test for muscle damage at that time was 24 hour urinary creatine excretion, and this was found to be raised in the 13 patients who were tested with a tendency for the urinary creatine to fall to normal levels as the patients recovered. The creatine phosphokinase enzyme test for muscle damage was not available at that time. Subsequently, it was found to be normal or only slightly elevated in ME suggesting that the disturbance is different from that found in other muscle diseases.

The illness had a striking resemblance to the disease described by Sigurdsson and others in Iceland during the winter of 1948–1949, and hence the name Iceland Disease was suggested for the illness.

In a leading article published anonymously in the Lancet in May 1956, Acheson reviewed eight similar outbreaks and suggested a title Benign Myalgic Encephalomyelitis for the new clinical entity based on the presumed underlying pathology.

He considered the disease to be "benign" compared with other epidemic infections of the nervous system seen in various types of encephalitis and in poliomyelitis due to the absence of patients dying. However, "benign" was later deleted from the title, leading to the abbreviation to ME, because in some cases the severity and duration of the disability resulting from the disease was far from being benign. He mentioned that hepatitis and

EPIDEMICS of ME (continued)

enlargement of the spleen might occur in addition to lymph gland involvement indicating the reticuloendothelial system participated in the clinical picture in some of the epidemics.

Alexis Shelokov and colleagues investigated an outbreak involving 50 student nurses and their tutors participating in residential courses at a psychiatric hospital near Washington DC, USA in 1953.

Half the patients had muscle weakness and poliomyelitis was suspected then eliminated. No other cause for the muscle weakness was found. All patients had features of a generalised illness similar to that described in patients with Iceland Disease. After the initial illness there was a subacute phase lasting several months consisting of episodes of feeling unwell and further muscle weakness.

Donald Henderson and Alexis Shelokov reviewed 23 similar epidemics in 1959. They found that the affected muscles were tender either diffusely or in focal discrete areas, which felt "oedematous, doughy or rubbery in consistence". They introduced the term Epidemic Neuromyasthenia, linking neurasthenia with myasthenia to describe the clinical picture. The term neurasthenia is unfortunate as it implies a disturbance of behaviour, which can follow an infection or be the result of stress, in the form of irritability and an inability to take exercise without excessive fatigue. Similar disturbances including crying spells without provocation are also seen during the convalescence of patients who have had strokes or head injuries. The association of similar behavioural disturbances with brain cell disorders such as cranial nerve palsies and hemiparesis with extensor plantar response is mentioned by Henderson and Shelokov (1959) as an occasional finding in some epidemics.

The association is clearly illustrated by Melvin Ramsay in a series of sporadic cases admitted to an infectious diseases department of a local hospital from the population of North West London in 1955 and 1956. Rather than labelling the illness neuromyasthenia a slight change to

neuronomyasthenia indicating a disease of nerve cells (or neurones) and muscle cells with muscle weakness might be more appropriate. Neurologists prefer to limit the term myasthenia to myasthenia gravis, a disorder of the neuromuscular junction which may present as a severe type of muscle weakness. In patients with Myalgic Encephalomyelitis/Neuronomyasthenia (ME/NM), "myasthenia mitis" has been used to describe a milder form of myasthenia in which muscle weakness develops during normal daily activities. Clinical tests were subsequently developed, which measure the declining muscle performance with activity and the slow recovery of muscle afterwards. In 1998 this delayed recovery of muscle function after a fatiguing isometric exercise test was confirmed in 1999 by Lorna Paul and colleagues.

MERGE has funded research which has revealed abnormalities in the function of blood vessels and blood cells. Abnormalities of blood vessels have been described in these epidemics of ME/NM. Infectious material was transferred from patients to monkeys during an epidemic in Adelaide, Australia in 1949–1950. The monkeys became ill and post-mortem examinations were carried out a month later. The only abnormalities discovered by Pellew and Miles (1955) were minute red spots along the course of the sciatic nerves.

Under the microscope the red spots contained localised collections of inflammatory cells, which had also infiltrated the area where the nerve roots come out of the spinal cord. The red colour of the spots was due to leakage of red blood cells. ME/NM is very rarely fatal so that a post-mortem study showing similar haemorrhages in humans is unique.

However, during the North of England epidemic in 1955 Andrew Wallis described the findings in a patient in her fifties, who developed the characteristic febrile illness leaving her debilitated and emotional. During the next fifteen months she continued to run a low grade fever with continued

EPIDEMICS of ME (continued)

mental deterioration before she died. The post-mortem revealed numerous small haemorrhages around blood vessels in the cerebral cortex extending into the mid-brain, which were considered to be the cause of her death.

These abnormalities may be found when patients die as the result of severe chronic alcoholism. This was not a factor in her case; she had had a febrile illness. Vasculitis involving the skin was recorded during outbreaks in Cumberland, Durham and North West London in 1955. A maculopapular rash may appear during the return of features of the initial illness such as flu-like symptoms and enlargement of lymph glands and liver. This skin overlying areas of localised muscle weakness may be affected at the time of these attacks.

In conclusion, Iceland Disease and ME/NM is a muscle/brain disorder, which occurs as clusters of cases in families, in institutions such as hospitals or schools, in districts as far apart as the northern townships in Iceland and Adelaide in Australia or sporadically. It is an infectious disease with an incubation period of 5 to 8 days. Acheson in 1959 used the expression "in a greater or lesser degree" to describe "the symptoms and signs of damage to the brain and spinal cord" in this disease. This expression can also be applied to the febrile illness and muscle involvement. Many patients recover and return to normal activities in weeks or months, while others have relapses with reactivation of features of the initial illness and further damage to new areas of the brain or muscles.

In extreme cases deterioration may lead to death. Muscle weakness has been measured in a few patients. After activity the recovery of muscle power is prolonged to an extent not recorded in any other disease. The association between these findings in muscle and vascular abnormalities in blood vessels and blood components needs exploring. For research purposes ME/NM patients with these physical signs should not be coupled with

patients whose main illness is chronic fatigue on exertion and who do not have these signs.

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WHAT I WANT FROM an ME SERVICE

This article appeared in our Journal and on IiME's web site in August 2007 and was written by Linda Crowhurst, a severely affected person with ME. As we plan to discuss the ME Clinic at the IiME Conference it was felt appropriate to republish this.

I need :

- Acknowledgement that ME is a WHO (ICD 10 - G93.3) defined neurological disease. An appropriate biomedical definition.
- Appropriate diagnostic criteria that acknowledge the wide number of specific physical symptoms.
- A biomedical clinician who can recognise the symptoms of ME and their impact. and make appropriate recommendations, based on current physical research.
- Appropriate biomedical tests and scans that prove that I have a physical illness and illuminate what is going wrong in my body.
- An appropriate biomedical assessment that will provide a medically-informed report about my illness and disability.
- Acknowledgement of severe disability so that support can be given to claim benefits and grants etc, to enable true entitlement.
- Careful testing and monitoring before any drugs are prescribed.
- Advice based on awareness to ensure safe practice and safe treatments regarding how to deal with other medical conditions and illnesses that might arise.
- The neurological symptoms to be explored , prioritised and validated.
- Access by phone for specific symptom management / backup.
- Home visits from a biomedical clinician.
- A service that is actively educating other clinicians and paramedical staff regarding the true physical nature and impact of this disease.
- The opportunity to choose to participate in

physical research so that people who have severe ME can be reflected in any research evidence compiled.

- A service that is particularly aware of the severity of my symptoms and the high level of post-exertional malaise and post-exertional fatigue I experience and can accommodate them; so that I can be seen and given proper ongoing support.
- The name "ME" to be used, as opposed to "CFS".

What I do NOT want from an ME Service

- A focus upon "fatigue".
- A "therapy"-led service
- To be included with undefined Chronic Fatigue illnesses and states.
- A psychosocial model of care.
- To be offered CBT and GET, as these are both dangerous and unsuitable for people with ME.
- To be patronised by medical professionals who do not believe that I have a physical disease .
- To be downgraded and treated as if my very real and severe neurological symptoms, such as paralysis, spasms, parasthesia and pain are insignificant or psychiatric in origin.
- To be offered psychiatric - originated management techniques , charading as treatment for this physical illness.
- To be described as "tired".
- Pretending to meet the needs of people with ME but actually working to a psychiatric paradigm.
- Any service based upon the Fukuda or Oxford criteria.



The 4th Invest in ME International ME/CFS Conference 2009



By Professor Malcolm Hooper

Conference Introduction

Invest in ME conferences have rightly become renowned for their high quality and eminent international speakers who have successively presented the most up to date biomedical information about this perplexing and devastating illness.

ME is a complex chronic multi-system illness, CMI.

Myalgic encephalomyelitis, muscle pain with inflammation of the brain and spinal cord, is a term that is both clinically meaningful and accurately descriptive of the nature of the illness. It has been known since 1934.

The name, first coined in 1956 by Donald Acheson who subsequently became Chief Medical Officer, was included, for the first time, in the World Health Organisation's International Classification of Disease in 1969 chapter G.93.3, neurological conditions.

To this day it is still so classified and the UK Government has stated that it accepts this classification although in every other way is acting and legislating to the contrary.

The introduction in 1988 of the alternative description, Chronic Fatigue Syndrome, CFS, describes only a symptom and has led to confusion, deception and obfuscation resulting in

Emeritus Professor of Medicinal Chemistry the University of Sunderland

Professor Hooper has published some 50 papers in peer-reviewed journals in the field of medicinal chemistry. He has served on committees of the Council for National Academic Awards (CNAA), the World Health Organisation (WHO) and the Science and Engineering Research Council (SERC).

He is a member of a number of learned bodies, including the Royal Chemical Society, the British Pharmacological Society and the Society for Medicines Research, where he has served on the committee for 12 years and served as Chairman for 2 years.

He was appointed Chief Scientific Advisor to the Gulf Veterans Association (GVA) and accepted by the Ministry of Defence (MoD) as their nominee on the Independent Panel established to consider the possible interactions between Vaccines and NAPS tablets. His involvement with the GVA brought contact with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (ME/CFS) and related disorders. Gulf War Illness/Syndrome (GWI/S) has much in common with ME/CFS.

He worked with the Autism Research Unit (ARU) at the University of Sunderland for over 20 years, leading to involvement in biochemical studies to offer help, support and treatment for people with autism. He served on the General Synod of the Church of England from 1970 to 1980 and he is a Christian Lay Leader, Preacher and Teacher.

The 4th Invest in ME International ME/CFS Conference 2009 *(continued)*

the sometimes acrimonious and bitter debates about the nature of the illness.

The imprecise word fatigue has been used by some psychiatrists to label ME as a behavioural and mental disorder. Such disorders are classified under F.48.0 which includes chronic fatigue and fatigue syndromes that are quite distinct from neurological conditions.

Today the diagnosis, treatment and management of ME are bedevilled by these two conflicting understandings of the illness leaving People with ME (PWME) frequently marooned, mistreated and misunderstood both medically and socially.



It is particularly apt that this 4th Conference is specially concerned with the severely disabled who have borne the brunt of the present obdurate, heartless and official views of ME that treat sick patients and their carers so cruelly.

It is a joy to welcome the speakers for this conference who come from the USA, Norway, Belgium as well as the UK.

The Whittemore-Peterson Institute, WPI, offers both challenge and hope to the world of ME with the "can do" energy and commitment so

typical of the American response to any daunting situation.

This Institute provides a working model of how to engage with ME and the growing number of complex CMI's that are emerging in today's world.

Annette Whittemore has provided the resources to bring the Institute into being and has an inspiring story to tell of how love, care and sheer 'guts' has realised a model for the rest of the world to follow.

Dan Peterson is the Medical Director of the WPI and has long wrestled with ME and provided hope, expert clinical care and understanding for numerous patients and carers for PWME.

The most severely disabled patients have suffered the greatest neglect. Exciting new possibilities for treatment that can change the lives of patients offer new hope for their future.

The third arm of the Institute involves research studies that address the nature of the illness and lay the foundations for new understanding and treatments of ME.

Judy Mikovits, Research Director of the WPI, presents her insights in to the diagnosis of the difficult and most complex ME cases. Diagnosis is the key to clinical treatment and definitions of ME are crucial for managing and effectively treating individual patients.

An institute that brings patients, clinicians and research workers together can provide a springboard for major advances in the ME. The WPI provides such a working paradigm and is a challenge to every country where ME is a major health issue.

John Chia has done great service by providing clear evidence of the role of enteroviruses in ME. Their role first identified by earlier workers in the field including, John Richardson, Irving Spurr, Byron Hyde and others, has been confirmed and extended by John's work.

His story makes it essential that the microbiological services that have been dismantled in this country must be re-established to support clinical need and research into

The 4th Invest in ME International ME/CFS Conference 2009 *(continued)*

effective treatments for enteroviral infections. Pooled human immunoglobulins are still effective in the very early stages of the illness, the first 6 months, but if this window of opportunity is missed then the illness may develop into a more chronic condition with serious consequences for the patient and the need for long drawn out and expensive therapy

Garth Nicolson has, at great personal cost, engaged with various CMLs and in the early days recognised the strong similarities between ME/CFS and Gulf War Syndrome. The recent Binn's report on Gulf War Illness clearly identifies the importance of chemical exposures in this CML although vaccine exposures may still play an important role. Chemical and biological exposures leading to neurodegenerative and neurobehavioural changes need to be better understood. Garth has provided effective antibiotic treatments for ME that follow some intracellular microbial infection, for example with mycoplasma organisms.

Previous Invest in ME conferences have emphasised the inadequacies of the current Fukuda/CDC definition of ME/CFS and the importance of sub-groups. Clarity is greatly needed in this area.

Norway, as a result of powerful and persistent campaigns by ME sufferers and activists led by Ellen Piro, has changed official attitudes towards ME by showing the effects of vaccines in provoking the illness which may also arise from natural infections.

Barbara Baumgarten heads a newly established ME-centre that provides correct diagnosis, treatment and management of ME emphasising once again the need for accurate diagnosis as the *sine qua non* for effective therapy for PWME. Will this new centre be the beginnings of a European WPI?

The seminal book by Hillary Johnson makes clear the need to consider the epidemiology of ME which is important for prompt action with regard to the illness. Although intracellular organisms, including rickettsia, chlamydia, borellia are well-known to give rise to ME the epidemiology of

Giardiasis, an extracellular parasite can teach us lessons that are valuable in engaging with ME.

Harald Nyland will make these interesting links in his presentation.

Kenny de Meirleir has championed patient needs and treatment in Europe and also contributed to the Canadian definition of ME/CFS. He has written perceptively about the disruption of essential immunological mechanisms in this illness by micro-organisms, heavy metals and other environmental chemicals. Case studies are the key to building up clinical understanding of the complexity of ME and its various manifestations that so perplex those newly encountering with this illness. We will learn much from his experiences.

Jonathan Kerr has carried out ground breaking studies in the genetics of ME especially in the most severely affected patients. This new field provides deeper understanding of the multi-system nature of the illness and shows how it can relate to other CMLs. The use of genetic analysis to identify clinical phenotypes for diagnosis and treatment will enable accurate sub-grouping of patients and targeted treatments to be developed and applied to this needy group of patients.

Jonathan's genetic studies show how a multiplicity of environmental insults can impinge upon a smaller number of key biochemical pathways and give rise to a multiplicity of symptoms – this is great gain and supports the experiences of many sick patients.

Basant Puri, also at great cost, has used advanced neuro-imaging techniques to investigate the structural and chemical changes in the brain associated with ME and devised useful treatments that specifically address these changes.

The multi-system nature of ME requires a conference Chairman who is familiar with the illness in all its manifestations. Jonathan Brostoff is such a person and has a vast experience in all the complexities of immunology and conducts research into allergy and environmental health issues.

The 4th Invest in ME International ME/CFS Conference 2009 *(continued)*

We are in for a splendid conference which provides real hope for all who suffer from ME and all those who care for them.

The medical and health community and, not least, medical and research administrators need to hear these stories and be prepared to learn from them, support biomedical research, and thereby serve the needs of sick patients.

In the UK we need an institute comparable to the WPI. When will the cry of sick patients and their carers be heeded and action taken to make effective treatment(s) available? When will money be allocated for biomedical research that addresses the real nature of this illness.

Much money has been devoted to support a model of ME that belittles patients, labels them with a diagnosis of a behavioural and mental disorder, and offers pacing (largely commonsense to people with any chronic illness), cognitive behavioural therapy, CBT, which even its strongest advocate state is "not remotely curative", and of doubtful efficacy, graded exercise therapy, GET, which makes many patients more ill (confirmed by biological studies), coupled with antidepressants which may provoke chemical sensitivities and are not necessary since many patients are not depressed.

This conference once again provides solid biomedical evidence which cannot continue to be ignored by health services increasingly wedded to an ideological, anti-clinical, and anti-scientific view of an illness that is now better understood and for which effective treatments following careful diagnosis are available.

Enjoy it!
Spread the message, challenge the bureaucrats, in Government, the NHS, and MRC and reclaim this field of medicine for both present and future patients.

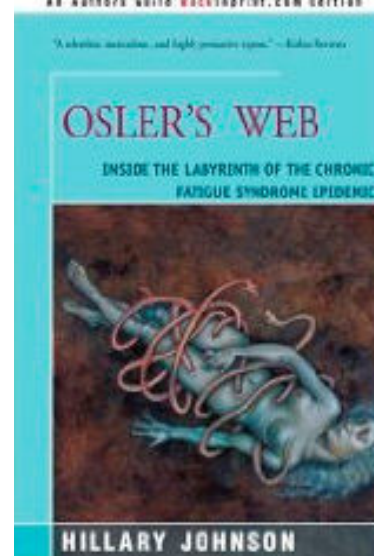
Malcolm Hooper
May 2009

OSLER'S WEB

To welcome **Hillary Johnson** to London we would like to highlight the later version of Osler's Web. This has been updated by Hillary. From the review by Maryann Spurgin at <http://www.cfids-cab.org/MESA/reviews4.html>

"..the most provocative portion of Johnson's discussion concerns the federal research establishment's attempt to manufacture a mental disorder out of a physical symptomatology. In meticulous detail, Johnson shows how bias in the choice of patients, value-laden selection of CFS-related data and prejudicial allocation of research funds permitted government researchers to conclude that CFS was a psychiatric condition, or rather, something more akin to a behavioral problem. If Johnson is correct, then the government's conclusion is a classic illustration of the Thomas Szasz thesis: The concept of mental illness is often a political tool with which society dismisses its inconvenient members."

Ms Spurgin states that one of Osler's Web's strong points is its illustration of a propaganda system at work where studies citing negative findings in CFS were readily published, whilst studies reporting positive physiological findings were turned down.



PROFILES of PRESENTERS at the INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

Conference Chair:

Professor Jonathan Brostoff MA DM DSc(Med) FRCP FRCPATH FIBiol

Jonathan Brostoff is Senior Research Fellow and Professor Emeritus of Allergy and Environmental Health at Kings College, London. He was the Foundation Professor of Allergy and Environmental Health and Director of the Centre for Allergy Research at University College London. Whilst at University College Hospital he was Physician in charge of the Allergy Clinic.

He is recognized as a leading international authority on food allergy and intolerance. Professor Brostoff was involved in one of the few, and much-quoted Spect scan studies of ME patients [Brainstem perfusion is impaired in patients with chronic fatigue syndrome. Costa DC, Tannock C and Brostoff J. *Quarterly Journal of Medicine* 1995;88:767-773].

Annette Whittemore

Founder and President of the Whittemore Peterson Institute for Neuroimmune Diseases, Reno, Nevada, USA.

Annette Whittemore graduated from the University of Nevada with a BS Ed in Elementary and Special Education. Teaching children who had neuro-cognitive deficits, like those found in autism, ADD, and learning disabilities, provided her with a unique experience to later use in her pursuit of answers to her daughter's serious illness.

Annette is the parent of a young adult who was severely affected by CFS and HHV-6. She and her husband are business owners and philanthropists in Reno and Sparks. Annette Whittemore is President and Co-founder of the foundation and became active in starting the HHV-6 foundation.

She started the foundation with Kristin Loomis from California after a brief meeting in Incline, NV. with Dr. Daniel Peterson, a leading clinical researcher in CFS and HHV-6.

When her daughter became ill with a chronic neuroimmune disease, Annette began to seek appropriate medical care. Annette found that few doctors understood the reasons for her daughter's continuing physical decline. For this reason, Annette has committed her time and resources to bringing attention to the serious nature of neuroimmune diseases and change her community in a positive way. She began this important mission in 1994 by supporting a Think Tank on ME/CFS, led by Dr. Daniel Peterson of Incline Village. In 2004 she and another patient advocate began a medical foundation to support research to find biomarkers of disease and treatments for patients impacted by the HHV-6A virus.

In order to provide solutions for patients and bring new doctors into this field of medicine, Annette, legislators, and others supported a bill to build a biomedical research center at the University of Nevada, Reno with an Institute for Neuro-Immune disease and the Nevada Cancer Institute. Annette founded the Whittemore-Peterson Institute for Neuroimmune Diseases which is being built on the medical campus with its mission to serve those with complex neuro-immune diseases such as ME/CFS, viral induced central nervous system dysfunction and fibromyalgia. In addition, Annette and Harvey have contributed over one million dollars and pledged another four million dollars in support of the building and programming to bring this project to fruition.



PROFILES of PRESENTERS at the INVEST in ME INTERNATIONAL ME/CFS CONFERENCE

As the Founder and President, Annette supports the basic and clinical research programs, recruitment of physicians and support personnel, while also leading fundraising activities. Researchers at the University of Nevada Medical School have also become collaborators on projects that are vital to our understanding of the immune deficits seen in these patients.

The Nevada Business Journal recently honored Annette and her husband Harvey as Health Care Heroes for their personal commitment to this Institute and its mission. Other community activities include current positions on the Governing Board of the Davidson Institute and the Community Board of Pack Paws (thanks to the HHV-6 Foundation and the WPI web site for this information).

Professor Garth Nicolson PhD

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Professor Garth Nicolson PhD (Biochemistry/Cell Biology),
President, Chief Scientific Officer and Research Professor, The Institute for Molecular Medicine;
Conjoint Professor, Faculty of Science and Technology, University of Newcastle, Newcastle,
Australia; Professor of Integrative Medicine, Capital University of Integrative Medicine,
Washington DC.

Professor Nicolson has been studying the role of infections in chronic illnesses such as Gulf War Syndrome, Chronic Fatigue Syndrome, Autoimmune and Degenerative Diseases for many years. He is also an extinguished cancer researcher and has many publications to his name, including 3 Current Content Citation Classics.

The Institute for Molecular Medicine is a research institute and its mission is to contribute to the understanding of and the prevention and cure of catastrophic human chronic diseases, such as autoimmune diseases, fatigue illnesses, rheumatic diseases, cancer, AIDS, and infectious and genetic diseases. This will be accomplished through innovative basic and translational research programs.

Presentation: Similar infections found in ME/CFS and Neurodegenerative and Neurobehavioral Diseases.

Garth L. Nicolson¹, Nancy L. Nicolson¹, Jorg Haier²

¹The Institute for Molecular Medicine, Huntington Beach, California,

²Department of Surgery, University Hospital, Munster, Germany

Objective: The majority of neurodegenerative diseases, fatiguing illnesses and neurobehavioral disease patients have chronic infections.^{1,2} Therefore, we examined the presence of certain co-infections in the blood of patients with Autism Spectrum Disorders (ASD) and compared these to ME/CFS patients.

Methods: North American ME/CFS and ASD patients were examined for various infections by isolation of leukocyte blood fractions and forensic polymerase chain reaction (PCR) to determine various infections.^{3,4}

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Results: ME/CFS patients (n=100, age=39.7±8.9) show evidence of multiple, systemic infections (Odds Ratio = 18.0, 95% CL 8.5-37.9, p< 0.001) that may be important in ME/CFS morbidity. ME/CFS patients had a high prevalence (51%) of 1 of 4 *Mycoplasma* species (OR = 13.8, 95% CL 5.8-32.9, p< 0.001) and often showed evidence of co-infections with different *Mycoplasma* species, *Chlamydia pneumoniae* (OR = 8.6, 95% CL 1.0-71.1, p< 0.01) and/or active Human Herpes Virus-6 (HHV-6) (OR = 4.5, 95% CL 2.0-10.2, p< 0.001). We found that 8% of the ME/CFS patients showed evidence of *C. pn.* and 31% of active HHV-6 infections.^{3,4} Recently we examined ASD patients (n=48, age 8.4±2.8) and found a large subset (58.3%) of ASD patients showed evidence of *Mycoplasma* species infections compared to age-matched control subjects (OR = 13.9, p<0.001). ASD patients also had *C. pn.* (4/48 or 8.3% positive, OR = 5.6, p<0.01) and HHV-6 (14/48 or 29.2%, OR = 4.5, p<0.01) infections in their blood.^{5,6}

Conclusions: The results indicate that similar to ME/CFS patients a large subset of neurobehavioral (ASD) disease patients show evidence of chronic infections. Although there were significant differences in median age and diagnoses between the two groups of patients, they tended to have similar incidence of three types of chronic infections: *Mycoplasma*, *Chlamydia* and HHV-6.

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4. Nicolson GL, Gan R, Haier J. Multiple co-infections (*Mycoplasma*, *Chlamydia*, human herpesvirus-6) in blood of chronic fatigue syndrome patients: association with signs and symptoms. *APMIS* 2003; 111:557-66.
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6. Nicolson GL, Gan R, Nicolson NL, et al. Evidence for *Mycoplasma*, *Chlamydia pneumoniae* and HHV-6 Co-infections in the blood of patients with Autism Spectrum Disorders. *J Neuroscience Res* 2007; 85:1143-48.

Prof Nicolson has published over 500 peer reviewed papers, among them current content citation classics. Here a couple of examples:

Metabolic syndrome and mitochondrial function: molecular replacement and antioxidant supplements to prevent membrane peroxidation and restore mitochondrial function. Nicolson GL.

J Cell Biochem. 2007 Apr 15;100(6):1352-69. Review. PMID: 17243117 [PubMed - indexed for MEDLINE]

Evidence for *Mycoplasma* ssp., *Chlamydia pneumoniae*, and human herpes virus-6 coinfections in the blood of patients with autistic spectrum disorders. Nicolson GL, Gan R, Nicolson NL, Haier J. *J Neurosci Res.* 2007 Apr;85(5):1143-8. PMID: 17265454 [PubMed - indexed for MEDLINE]

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Professor Harald Nyland MD, PhD

Institute of Clinical Medicine, Department of Neurology, Haukeland University Hospital, 5021 Bergen, Norway

On 20 July 2006 Professor Nyland was knighted by the King of Norway for his services for MS research and treatment of MS patients. Since the 1970s he has built up a large multidisciplinary research team at Haukeland University Hospital which has worked with immunological diseases in the brain and other parts of the nervous system. Professor Nyland has published over 100 scientific papers in international publications, either as the main author or as a senior co author. He has also taught neurology students for more than 20 years. Thanks to Professor Nyland's considerable input the Neurology Department at Haukeland University Hospital is at present a national centre of excellence for MS in Norway. Dr Nyland graduated in 1968 and took his medical PhD in 1982. He has also been strongly involved with ME patients for more than 10 years and during this time he has examined over 1500 patients with suspected ME.

Presentation:

Epidemics & ME: Lessons from the Giardia epidemic in Norway

Background

In 2004 a few thousand people contracted a gastrointestinal infection due to consumption of contaminated public drinking water (1). According to Nygard et al. (2), approximately 48,000 people were exposed to the contaminated tap water during the outbreak. People affected had been drinking tap water from the public waterworks supplying the inner city of Bergen, a coastal city of western Norway, during the outbreak.

Leaking sewage pipes combined with insufficient water treatment were the likely causes of the epidemic (1). The outbreak probably began in August and peaked in early October (2). A total of 1300 laboratory-confirmed cases of *Giardia duodenalis* were reported (1). In addition one could expect a number of asymptomatic carriers as well (3). It took about six to eight weeks before the medical community and local health authorities acknowledged the epidemic and identified the parasite, *G. lamblia*, as the cause of the gastrointestinal infection (4). One reason for the late detection of the cause is probably that *G. lamblia* is non-endemic in Norway and therefore not normally tested for (2).

The people infected were mostly women and younger people (2, 4) who had been drinking larger amounts of tap water, often more than five glasses per day (2). The municipality of Bergen city accepted responsibility for the insufficient quality of the water supply and their insurance carrier is expected to pay compensation. Most cases are still being arbitrated, and some may end up in court.

G. lamblia is one of the most common causes of protozoally-induced diarrhoea in humans globally (1, 5), but in Norway before 2005, this infection was mainly associated with people travelling to "exotic" places, as more than 90 % of yearly confirmed cases are imported by foreign travellers (5). This outbreak of giardiasis is the largest waterborne outbreak in recent time (5), and the first reported giardiasis outbreak of epidemic proportion in Norway (6).

An outbreak of this size is unusual in the Nordic countries, and even in Europe. Information from the Norwegian Prescription Database revealed that probably more than 2,500 cases were

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treated for giardiasis, likely associated with this epidemic (2).

Most of the affected patients responded well to standard treatment with antibiotics, although for some only one cure was not sufficient to clear the parasite from the body (4). After treatment some returned to their general practitioners because they experienced recurring symptoms (5). Following the Bergen giardiasis epidemic a few hundred developed post-infectious irritable bowel syndrome [PI-IBS] (8), and many still experienced abdominal symptoms and prolonged fatigue two years after the initial infection (9).

Around 2005 and 2006, severely fatigued patients started to be referred to a neurologist specialising in chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) for further investigation. The majority of the fatigued patients subsequently participated in an educational programme in the fall of 2007, focusing on following aspects: post-infectious prolonged fatigue (disease knowledge); physical activity; psychological aspects accompanying severe illness; nutrition; legal entitlements administered by the Norwegian Labour and Welfare Administration, as well as future plans for a rehabilitation programme aimed to facilitate recovery and return to work or education.

After a thorough examination, 58 persons fulfilling the 1994 Fukuda et al. (10) criteria for chronic fatigue syndrome were consecutively enrolled in a prospective multidisciplinary research project (11). Data show that among this subgroup of severely fatigued persons, some had become acutely fatigued (25%), some after a few weeks (14.3%), and some more gradually over several months (60.7%). The multidisciplinary research project's main objectives are: 1) Present the clinical findings for the group of patients with post-infectious fatigue syndrome and to determine symptomatic and functional status during a 5-year follow-up; 2) Explore and describe the patients' own experience of living with this condition and being in a rehabilitation process. The research study being presented in this paper is focusing on the human aspects of living with giardiasis.

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Additional examples of papers by Professor Nyland: -

Vaccination as teenagers against meningococcal disease and the risk of the chronic fatigue syndrome. Magnus P, Brubakk O, Nyland H, Wold BH, Gjessing HK, Brandt I, Eidem T, Nøkleby H, Stene-Larsen G. *Vaccine*. 2009 Jan 1;27(1):23-7. Epub 2008 Nov 5. PMID: 18984023 [PubMed - indexed for MEDLINE]

Vitamin D-dependent rickets as a possible risk factor for multiplesclerosis. Torkildsen Ø, Knappskog PM, Nyland HI, Myhr KM. *Arch Neurol*. 2008 Jun;65(6):809-11. PMID: 18541802 [PubMed - indexed for MEDLINE]

Dr. Jonathan Kerr

Jonathan Kerr was born in Belfast in 1963, qualified in medicine from Queen's University of Belfast (1987), and completed training as a medical microbiologist (1995). He has worked as a microbiologist in Belfast, Manchester and London, taking up post as a Consultant Senior Lecturer in Microbiology at Royal Brompton Hospital / Imperial College in June 2001, and then Sir Joseph Hotung Clinical Senior Lecturer in Inflammation at St George's University of London in 2005.

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

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

Dr. Jonathan Kerr and colleagues at St. George's University of London reported in the July 27, 2005 issue of the *Journal of Clinical Pathology* that a preliminary study of 25 CFS patients and 25 matched healthy controls revealed abnormalities in 35 of 9,522 genes analyzed using microarray technology. Polymerase chain reaction studies showed the same results for 16 of these genes. Dr. Kerr has recently defined seven genomic subtypes of CFS based on 88 genes that are expressed differently in CFS patients than they are in normal controls.



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

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

Conference Presentation: Microbial infections in eight genomic subtypes of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME)

Lihan Zhang,¹ Beverley Burke,^{1*} Robert Petty,^{1*} John Gough,¹ David Christmas,² Derek L Matthey,³ Selwyn CM Richards,⁴ Janice Main,⁵ Derek Enlander,⁶ David Honeybourne,⁷ Jon G Ayres,⁷ David J Nutt,² Jonathan R Kerr.¹

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³Staffordshire Rheumatology Centre, Stoke on Trent, UK; ⁴Dorset CFS Service, Poole Hospital, Dorset, UK; ⁵Dept of Infectious Diseases and General Medicine, Imperial College London, St Mary's Hospital, London, UK; ⁶New York ME / CFS Service, 860 Fifth Avenue, New York, USA; ⁷Dept of Respiratory Medicine, Birmingham Heartlands Hospital, UK

Reprints or correspondence: Dr Jonathan R Kerr, Room 2.267, Jenner Wing, St George's University of London, Cranmer Terrace, London SW17 0RE, UK. Email: jkerr@sgul.ac.uk.

Abstract Jonathan Kerr

We have previously reported abnormal expression of 88 human genes in the blood of patients with Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME) and 7 genomic subtypes of CFS/ME (Kerr JR, et al. J Infect Dis 2008;197:1171-84). In this study we attempted to reproduce our previous findings in 59 new CFS patients, to determine expression levels of these genes in patients with endogenous depression, and to test the hypothesis that particular microbial infections are associated with particular genomic CFS subtypes.

We determined expression levels of 88 human genes in blood of 53 new patients with idiopathic CFS/ME (according to Fukuda criteria), 6 patients with Q-fever associated CFS/ME (Q-CFS/ME) from the Birmingham Q-fever outbreak (according to Fukuda criteria), 14 patients with endogenous depression (according to DSM-IV criteria) and 18 normal blood donors. In patients with CFS/ME differential expression was confirmed for all 88 genes. Q-CFS/ME patients had similar patterns of gene expression to idiopathic CFS/ME. Gene expression in endogenous depression patients was similar to that in the normal controls, except in the case of four genes (APP, GNAS, PDCD2, PDCD6), where significant upregulation (fold-difference ≥ 1.5) was noted.

Taqman PCR delta Ct values for 88 genes in CFS/ME patients in the present study (n=59) and our previous study (n=55) were combined resulting in a gene database of 117 CFS/ME patients. Clustering revealed 8 genomic subtypes with distinct differences in SF-36 scores, clinical phenotypes, severity and geographical distribution. Antibody testing for Epstein-Barr virus (EBV), enterovirus, *Chlamydia pneumoniae*, *Coxiella burnetii* and parvovirus B19 revealed significant subtype-specific relationships for EBV and enterovirus, the two most common infectious triggers of CFS/ME.

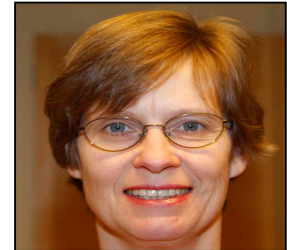
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Additional links for Dr Kerr:

Jonathan Kerr, Seven genomic subtypes of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME): a detailed analysis of gene networks and clinical phenotypes. J Clin Pathol. 2007 Dec 5. ub ahead of print] PMID: 18057078 [PubMed - as supplied by publisher]

Dr. Barbara Baumgarten MD

Project leader , ME/CFS-center, Oslo University Hospital, Ullevål
Dr Barbara Baumgarten was born in Hamburg, Germany, and moved to Norway in 1980. She studied medicine at the University of Oslo and from 1992-93 she worked at a hospital in internal medicine and surgery. From 1993 she has been working in General Practice, with a two year assignment at a nursing home.



Since 1996 she has had her own practice and has been seeing patients with ME since 1997. From April 2006 she has been working one day a week as a GP at the department for infectious diseases, Ullevål University Hospital, Oslo. Her work there was to look at the need of specialized medical services for ME-patients. That has resulted in a new ME-clinic. Since August 2008 her main job at Ullevål University Hospital has been leader for the new ME-centre, which was officially opened on December 11th 2008.

The ME Centre in Oslo is unique in that patients have been closely involved in its formation. Dr Baumgarten has given many lectures about ME for GP's, at hospitals and for the Norwegian ME Association. She is a board member at the Oslo branch of the Norwegian Medical Association.

Presentation Dr. Baumgarten: Services for correct diagnosis and Management/Treatment of ME

Thanks to the ME-patient organizations in Norway, Norwegian politicians have become aware of the problems ME patients face, both concerning diagnosis and treatment of their condition. Some years ago there were only a few doctors who knew enough about Post infectious fatigue syndrome, as it was most commonly called then, to set the diagnosis. One of the doctors who would recognize the condition was Dr. Oddbjørn Brubakk who was head of the department for infectious diseases at Ullevål University Hospital in Oslo. Two patients had approached him in 2003 and asked if it was possible to start a coping course for patients with ME since there was little other treatment to offer them. A group including the patient representatives and professionals from the medical division and the Patient education center at Ullevaal started working on a concept for a course that has been running twice a year since 2004. Therefore, when political awareness around ME was growing Ullevaal University Hospital was asked by the Eastern Norway Regional Health Authority to have a closer look at the needs of that patient group. Since 2006 I have been working on a concept for a ME-clinic and last year we got funded by the South-Eastern Norway Regional Health Authority to start the clinic as a project. We have today an out-patient clinic where patients can come to get diagnosed, and where they can get help in coping with ME by a multi professional team that includes an occupational therapist, a physiotherapist, a dietitian and a social worker. Patients get help to learn energy economizing, relaxation techniques, dietary advice and advice with their problems with the social security system. When working on the concept I became aware that the permanently bedbound patients wouldn't be able

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to come to our clinic. So I introduced the concept of an ambulatory team that could go home to people helping to get the correct diagnosis and offering them the same advice with up to five visits by two from the team each time. The limitation is that we must be able to do the visit in one day including transportation, so we cover only eastern Norway. These services have just started and now the South-Eastern Norway Regional Health Authority have asked Oslo University Hospital, Ullevaal (three University hospitals in Oslo joined by January 1st 2009) to investigate the possibility of starting an in-patient service for severe ME-sufferers, which would cover the whole country. The ward would provide the possibility for careful examination to rule out all other conditions that might explain the condition and give those who can profit from treatment/coaching that possibility.

Our biggest concern at this time is that patients with very severe ME will be too ill to be moved to the ward and might become worse by physical examinations.

The report is handed over to the authority by April 30th and we hope to have an answer by mid June.

Professor Kenny De Meirleir MD PhD

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



He assesses/treats 3,000 to 4,000 ME/CFS patients annually. Professor Kenny L. De Meirleir, MD received his medical degree at Vrije Universiteit Brussel, Magna cum laude. His research activities in Chronic Fatigue date back to 1990. His other research activities in exercise physiology, metabolism and endocrinology have led to the Solvay Prize and the NATO research award. He is director of the Himmunitas Foundation Brussels and Professor at the Vrije Universiteit Brussel, as well as consultant in the Division of Cardiology and director of the cardiac rehabilitation program at Vrije Universiteit Brussel.

Presentation Professor De Meirleir:

Research on Eextremely Debilitated M.E. Patients Reveals the True Nature of the Disorder

Kenny De Meirleir(1), Chris Roelant(2), Marc Fremont(2), Kristine Metzger(2), Henry Butt(3)

(1) Vrije Universiteit Brussel & HIMMUNITAS foundation, Brussels, Belgium

(2) Protea Biopharma, Brussels, Belgium

(3) Bioscreen & Bio 21, University of Melbourne, Melbourne, Australia

In this study we compared totally bedridden patients (Karnofski score 20-30) with less ill ME patients (Karnofski score 60-70), family controls, contact controls and non-contact controls. EBV, HHV6 and Borna virus titers were not different in the three groups. Plasma LPS distinguished the groups, with the highest values in the bedridden patients. LPS is a strong activator of the immune system and high plasma concentrations suggest a hyperpermeable gut. There are many possible causes for this, but a lack of 'local' energy production is one of them. In a separate study (In Vivo, in press) we observed intestinal overgrowth of Gram positive D/L lactate producing

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bacteria which are also known to produce H₂S in presence of certain heavy metals as a survival defense mechanism. We therefore hypothesized that the urine of the bedridden ME patients would contain more H₂S derived metabolites than the less ill and the controls. Using a proprietary simple colorimetric urine test this hypothesis was confirmed.

In the extremely ill, urine added to the yellow color reagent immediately turns dark blue, whereas in the less ill the reaction is slower and in the controls no reaction occurs.

Being a potent neurotoxin, H₂S induces photophobia, intolerance to noise, mitochondrial dysfunction by inhibition of cytochrome oxidase, depresses the cellular immune system and induces neutropenia and low numbers of CD8+ lymphocytes. Its effects, at least in part explain the clinical condition of the severely disabled ME patients.

Furthermore bacterial H₂S induces increased ROS production by the liver and retaining of heavy metals, particularly mercury, in the body. Mercury is also neurotoxic, induces apoptosis and interferes with the aerobic metabolism. Chronic increased production of H₂S by intestinal bacteria leads to build-up of mercury in the body as proven by a Zn DTPA/DMPS challenge test. In about 20% of the ME patients (the most severely ill) we observed using a special luminescence technique the formation of proteins with aberrant conformation which interfere with the energy metabolism.

In conclusion, ME is a disorder which is caused by increased endogenous H₂S production. H₂S initiates a chain of events in the body, with more and more negative effects on the aerobic metabolism and depression of the immune system leading to higher rates of infections and reactivation of endogenous viruses. In the most severe cases of the disease proteins with aberrant conformation may develop which put the patients in a total energy depleted state.

Examples of other papers from Professor De Meirleir include –

Lower frequency of IL-17F sequence variant (His161Arg) in chronic fatigue syndrome patients. Metzger K, Frémont M, Roelant C, De Meirleir K. Biochem Biophys Res Commun. 2008 Nov 7;376(1):231-3. Epub 2008 Sep 5. PMID: 18774769 [PubMed - indexed for MEDLINE]

Unravelling intracellular immune dysfunctions in chronic fatigue syndrome: interactions between protein kinase R activity, RNase L cleavage and elastase activity, and their clinical relevance. Meeus M, Nijs J, McGregor N, Meeusen R, De Schutter G, Truijen S, Frémont M, Van Hoof E, De Meirleir K. In Vivo. 2008 Jan-Feb;22(1):115-21. PMID: 18396793 [PubMed - indexed for MEDLINE]

Dr. Daniel Peterson MD

Daniel Peterson is a graduate Magna cum Laude, Phi Beta Kappa of Carleton College in Northfield, Minnesota. He graduated from the University of Rochester School of Medicine in Rochester, New York, in 1976. Dr. Peterson served his internship and residency at the University of Utah Medical Center from 1976-1979 and became a Diplomat of the American Board of Internal Medicine in 1979.



He has been caring for patients with Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS), for two decades, and his clinical work is complimented by a strong commitment to research as evidenced by his participation in more than 17 research studies, numerous drug trials and his foresight to collect and maintain the world's single largest repository of ME/CFS patient samples. Dr. Peterson was on the founding board of the IACFS. Among the numerous awards that he has received, in 2007 he was awarded the prestigious Nelson Gantz Clinician Award.

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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.

Dr Peterson is an affiliate of the Sierra Internal Medicine Associates in Incline Village, Nevada; ME/CFS researcher and clinician; a board member of the American Association for Chronic Fatigue Syndrome; and member of the International Chronic Fatigue Syndrome Study Group. Dr Peterson was one of the two physicians who identified the original outbreak of CFS in Incline Village, Nevada, in 1984. (thanks to the WPI web site for this information).

Conference Presentation: Treatment Regimes for the Most Severe Cases

Chronic Fatigue Syndrome/ME is a worldwide problem with incidence of approximately 700 people per 100,000.

A subset of patients diagnosed with CFS/ME are severely affected with marked resultant disability and reduced quality of life. In addition to clinical symptoms, these patients can be assessed through objective markers and further categorized by degree of disability and severity of illness. In addition to functional studies, biological markers exist, they are useful in establishing baseline values and used to follow treatment regimens.

It is important to thoroughly evaluate these patients in order to rule out comorbid conditions that are also treatable and to establish subsets allowing targeted interventions and rehabilitation strategies. A diagnostic algorithm has been developed to identify this group of patients and to facilitate aggressive treatment strategy. Biological markers can include genetic studies for predisposition to ME, extensive immunological profiling to document perturbations of B-cell and T-cell function and gene expression arrays.

Additionally, platforms exist to look for pathogenetic mechanisms including viral arrays and cytokine analysis. Neuroimaging can further determine objective markers of CNS dysfunction. Functional studies employed include studies of VO2 max and neurocognitive testing. Generally, these severely affected subsets of patients have been ill for prolonged period of time and have a guarded prognosis. However, dramatic results have been reported with aggressive targeted strategies. A team approach is required in order to provide necessary services including in-home services, hospitalization, and aggressive management for orthostatic intolerance, cognitive dysfunction, and immune perturbations.

Objective markers are followed throughout this process to gauge effectiveness of therapy and axillary supportive services are instituted concomitantly to address issues of secondary mood disorder, deconditioning, and psychosocial dysfunction related to chronic illness.

A center of excellence model is currently being developed to implement this broad approach to the most severely disabled patients that include translational research from the laboratory to the

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bedside and includes not only diagnostics but appropriate drug development or alternative interventions.

Daniel L. Peterson, M.D.

DLP/ldr/rsu

D: 05/18/09

T: 05/19/09

Professor Basant Puri MD, PhD

**Professor and Consultant, MRC Clinical Sciences Centre,
Hammersmith Hospital, Imperial College School of Medicine**

Professor Basant K. Puri is both a medical practitioner, working as a consultant at Hammersmith Hospital in London, and a senior scientist, working at Imperial College London.

He is head of the Lipid Neuroscience Group at Imperial College and is the author of over 130 peer-reviewed medical and scientific papers and over 30 books.



Conference Presentation: Neuro-Imaging – Research of ME patients

In this talk, the results of recent proton neurospectroscopy and high-resolution structural magnetic resonance imaging studies of myalgic encephalomyelitis carried out at Hammersmith Hospital, London, will be described.

Additional links for Professor Puri –

Serial structural MRI analysis and proton and ³¹P MR spectroscopy in the investigation of cerebral fatty acids in major depressive disorder, Huntington's disease, myalgic encephalomyelitis and in forensic schizophrenic patients. Puri BK, Tsaluchidu S, Treasaden IH. World Rev Nutr Diet. 2009;99:31-45. Epub 2009 Jan 9. Review. No abstract available. PMID: 19136837 [PubMed - indexed for MEDLINE]

High-resolution magnetic resonance imaging sinc-interpolation-based subvoxel registration and semi-automated quantitative lateral ventricular morphology employing threshold computation and binary image creation in the study of fatty acid interventions in schizophrenia, depression, chronic fatigue syndrome and Huntington's disease. Puri BK. Int Rev Psychiatry. 2006 Apr;18(2):149-54. Review.

Proton and ³¹-phosphorus neurospectroscopy in the study of membrane phospholipids and fatty acid intervention in schizophrenia, depression, chronic fatigue syndrome (myalgic encephalomyelitis) and dyslexia. Puri BK. Int Rev Psychiatry. 2006 Apr;18(2):145-7. Review. PMID: 16777668 [PubMed - indexed for MEDLINE]

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Dr John Chia MD

Dr Chia is an infectious disease specialist practicing in Torrance, California, USA and has published research recently (**Chronic fatigue syndrome associated with chronic enterovirus infection of the stomach**) on the role of enteroviruses in the aetiology of ME/CFS – an area which has been implicated as one of the causes by a number of studies. There are more than 70 different types of enteroviruses that can affect the central nervous system, heart and muscles, all of which is consistent with the symptoms of ME/CFS. By analyzing samples of stomach tissue from 165 patients with CFS,



Dr. Chia's team discovered that 82% of these individuals had high levels of enteroviruses in their digestive systems. Dr Chia's research may result in the development of antiviral drugs to treat the debilitating symptoms of ME/CFS.

Conference Presentation from Dr Chia:

Diagnosis and Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Associated with Chronic Enterovirus infection. John Chia, Andrew Chia. EV Med Research

ME/CFS is an elusive illness without a clear etiology and treatment. Emerging evidences suggest that enteroviruses can persist in the tissues of ME/CFS patients and may be responsible for the various symptoms. Enteroviruses are common causes of respiratory, gastrointestinal and non-specific flu-like illnesses. Major epidemics of enterovirus infections including but not limited to meningoencephalitis, myocarditis, pleurodynia, myositis and hand-foot-mouth diseases have been well-documented in the past decades.

In some cases, acute enterovirus infections can cause CD8+ T lymphocytopenia predisposing to reactivation of endogenous herpes viruses. Initial isolation of enteroviruses from patients with acute infections followed by demonstration of persistent viral infection in tissues years after the patients developed chronic symptoms lends support to the pathogenic role of enteroviruses in ME/CFS.

Presumptive clinical diagnosis of chronic enterovirus infection requires a high index of suspicion, familiarity with the protean manifestations of acute infections and understanding of chronic viral persistence.

There is not yet a specific diagnostic test for ME/CFS. Significantly elevated neutralizing antibody titer over time suggests persistent immunologic response to specific enterovirus(s) infection in the tissues. Neutralizing antibody test for 11 of the most common non-polio enteroviruses is performed by one U.S. reference laboratory.

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In contrast to other types of viremic infections, EV RNA levels in whole blood of ME/CFS patients are extremely low, which likely explain the discrepancy of results reported from different research laboratories over the past two decades.

Immunoperoxidase staining for viral protein in the stomach biopsies is more sensitive than the neutralizing antibody test or EV RNA detection, and furthermore, demonstrates the antigens in tissues where viruses are expected to replicate and persist based on the route of transmission.

The finding of enteroviral RNA and growth of non-cytopathic viruses from the same tissues support the validity of protein staining.

As enteroviruses have been largely forgotten since the eradication of poliomyelitis through effective vaccination, there is no specific antiviral therapy for acute or chronic infections. Pleconaril, an anti-capsid agent, showed limited benefit in 1/4 patients with ME/CFS associated with chronic enterovirus infections.

Intravenous immunoglobulin, given monthly or every few months, can ameliorate inflammatory symptoms in less than 1/3 of adult patients, but may be more effective in pediatric patients. The combination of alpha and gamma interferon can induce short-term remission in about 45% of ME/CFS patients with debilitating myalgia, but is quite expensive and often poorly tolerated.

One of the Chinese herbs, oxymatrine, has beneficial effect in 52% of 300 ME/CFS patients, but transient increase in symptoms are expected in most of the patients.

Cytokine gene expression study during therapy demonstrates an increase of IL12/IL10 ratio in 7/7 responders but in 0/10 non-responders. A decrease of stainable enteroviral protein is demonstrated in the stomach biopsies of three responders on oxymatrine therapy.

Previous evidence for enterovirus infection in ME/CFS from over a decade ago has been confirmed and extended in recent studies. Development of antiviral therapy against enteroviruses is paramount; and the importance of enteroviruses in ME/CFS can be realized with a randomized, placebo-controlled antiviral drug trial.

Additional links for Dr Chia:

John Chia, Chronic fatigue syndrome is associated with chronic enterovirus infection of the stomach. J Clin Pathol. 2008 Jan;61 (1):43-8. Epub 2007 Sep 13. PMID: 17872383 [PubMed - indexed for MEDLINE]

Enterovirus infection as a possible cause of pityriasis rosea: demonstration by immunochemical staining. Chia JK, Shitabata P, Wu J, Chia AY. Arch Dermatol. 2006 Jul;142(7):942-3. No abstract available. PMID: 16847226 [PubMed - indexed for MEDLINE]

Diverse etiologies for chronic fatigue syndrome. Chia JK, Chia A. Clin Infect Dis. 2003 Mar 1;36(5):671-2; author reply 672-3. No abstract available. PMID: 12594650 [PubMed - indexed for MEDLINE]

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Dr Judy Mikovits PhD

Dr. Mikovits obtained her Ph.D. in Biochemistry and Molecular Biology from George Washington University. Dr. Mikovits served as a senior scientist at Biosource International, where she led the development of proteomic assays for the Luminex platform that is used extensively for cytokine activity assessment in therapy development.

Dr. Mikovits spent more than 20 years at the National Cancer Institute in Frederick MD during which time she received her PhD in



Biochemistry and Molecular Biology, investigating mechanisms by which retroviruses dysregulate the delicate balance of cytokines in the immune response. This work led to the discovery of the role aberrant DNA methylation plays in the pathogenesis of HIV. Later in her career at the NCI, Dr. Mikovits directed the Lab of Antiviral Drug Mechanisms (LADM) a section of the NCI's Screening Technologies Branch in the Developmental Therapeutics Program. The LADM's mission was to identify, characterize and validate molecular targets and to develop high-throughput cell-based, genomic and epigenomic screens for the development of novel therapeutic agents for AIDS and AIDS-associated malignancies (Kaposi's sarcoma). Formally trained as a cell biologist, molecular biologist and virologist, Dr. Mikovits has studied the immune response to retroviruses and herpes viruses including HIV, SIV, HTLVI, HERV, HHV6 and HHV8 with a special emphasis on virus host cell interactions in cells of the hematopoietic system including hematopoietic stem cells (HSC).

Dr. Mikovits' commercial experience includes serving as a senior scientist and group leader at Biosource International, where she led the development of proteomic assays for the Luminex platform that is used extensively for cytokine activity assessment in therapy development. She also served as Chief Scientific Officer and VP of Drug Discovery at Epigenx Biosciences, where she led the development and commercialization of cell and array-based methylation assays for drug discovery and diagnostic development.

She is Research Director at the Whittemore Peterson Nevada CFS centre for Neuro-Immune disorders and has co-authored over 40 peer reviewed publications that address fundamental issues of viral pathogenesis, hematopoiesis and cytokine iology. (thanks to the WPI web site for this information).

Conference Presentation Dr Mikovits:

Translational Research Towards the Diagnosis of Difficult and Complex Medical Cases of ME/CFS

The research program of the Whittemore Peterson Institute is unique in that it has taken a systems biology approach to the study of CFS. This approach involves profiling a patient with respect to genetics, immune system phenotype and function and expression of viruses. Both research and clinical data are entered into a central database for correlation with clinical

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data. These data are then translated into diagnostic and treatment strategies that can be personalized" for each patient. This model can be extended to each physician such that data from individual cohorts or subgroups of patients can be entered into a fully secure/ international national database that can be queried by physicians anywhere in the world giving each physician tools with which to diagnose and treat patients with similar genetic, immune and pathogen profiles. We used this strategy to study more than 100 difficult and complicated CFS patients from a well-defined Nevada ME/CFS cohort resulting from outbreak of ME/CFS that occurred between 1984 and 1987. Immune profiling reveals immune defects including in T, B and NK cell compartments.

These abnormalities are suggestive of a persistent infection and predicative of the development of lymphoma. Moreover using antibody microarrays to profile serum biomarkers in this cohort we have developed a five-cytokine/chemokine signature that can identify CFS patients from controls with 94% sensitivity and specificity. Viral microarray studies demonstrate persistent active herpes viruses, enteroviruses, adenoviruses and parvoviruses. Genetic profiling revealed HLA and killer immunoglobulin receptor (KIR) genotypes predictive of susceptible and protective genotypes in this cohort. Taken together these data suggest that this systems biology strategy can be developed diagnostically, for the development of serum biomarkers to stratify subgroups of ME/CFS patients for appropriate anti-inflammatory, antimicrobial and antiviral therapeutics.

Additional links for Dr Mikovits: <http://lib.bioinfo.pl/auth:Mikovits,J>

Example of other work:

Epigenetic control during lymphoid development and immune responses: aberrant regulation, viruses, and cancer. Muegge K, Young H, Ruscetti F, Mikovits J. Ann N Y Acad Sci. 2003 Mar;983:55-70. Review.

PMID: 12724212 [PubMed - indexed for MEDLINE]



The Invest in ME International ME/CFS Conferences

Invest in ME

International ME/CFS 29th May 2009 Conference

Agenda

07:45	Registration	
08:55	IiME Welcome	IiME
09:00	Welcome	Professor Brostoff
09:05	Key Note Speech	Annette Whittemore
09:35	Similar infections found in ME/CFS and Neurodegenerative and Neurobehavioral Diseases	Professor Garth Nicolson
10:25	Epidemics & ME: Lessons from the Giardia epidemic in Norway	Professor Harald Nyland
10:55	Coffee/Tea Break	
11:15	Microbial infections in eight genomic subtypes of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME)	Dr Jonathan Kerr
11:45	Services for correct diagnosis and Management/Treatment of ME – including ambulatory services for severe ME	Dr Baumgarten
12:15	The ME Clinic - Discussion	Professor Brostoff + Presenters
12:30	Lunch	
13:25	Research on extremely debilitated M.E. patients reveals the true nature of the disorder	Professor Kenny De Meirleir
14:10	Treatment Regimes for the Most Severe Cases	Dr Dan Peterson
14:55	Neuro-Imaging – Research of ME patients	Professor Basant Puri
15:10	Coffee/Tea Break	
15:30	Diagnosis and Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Associated with Chronic Enterovirus infection	Dr John Chia
16:15	Research and Diagnosis of difficult and complex medical cases of ME	Dr Judy Mikovits
17:00	Plenary Session	Professor Brostoff + Presenters
17:00	Adjourn	