t in ME – Research International ME Conference 2016
ME C11 2016

e, 2016, I was privileged to attend the 11th Invest in ME – Research International conference in London - the theme being
Invest in ME - Research".
ence was held at a wonderful venue, at number 1, Great George St, Westminster. This provided space, and being all on on
well to those with ME/CFS. And we could look upwards at the magnificent painted ceiling during breaks. The conference
ll attended by those with ME/CFS, carers, advocates, doctors and researchers. 18 countries were represented.

ence was opened by Dr Ian Gibson with a brief overview of 10 years of research, with the comment that research is now f
we are entering a new dawn. ME/CFS is a global problem, needing much more funding and education. There needs to be
the United Nations. In Britain a Centre of Excellence is proposed.

eaker was **Dr Vicky Whittemore**, (Programme Director in the National Institute of Neurological Disorders at the NIH,
re has been 5 years of research into ME/CFS at the NIH, leading to a new vision for research in the USA. The NIH is one
27 institutes and centres. There is intramural research within the NIH campus and extramural research going on elsewher
ural protocol for ME/CFS research is headed by Dr Avindra Nath. They are planning to recruit 40 postinfectious ME/CF
ears of onset). There will be extensive analysis using biospecimens. Additional cohorts are envisaged.
group was revitalised in 2015, to develop long, intermediate and short term goals, with strategies to support and stimulate
ims include: fostering international collaboration, setting research priorities, supplementing grants etc. Research funding
5-6 million annually over the past 8 years, and there is much room for growth. The NIH needs information, and needs to
eeds and opportunities. New young researchers are to be encouraged, with patient engagement and support from academi
term: research will be expanded, new treatments developed, with support for clinical trials and the aim should be improve
hose with ME/CFS.

Olli Polo (Tampere, Finland) is a pulmonary medicine specialist working in the area of sleep, apnoea and fatigue. He has
atients. His main opening message was how to get GPs to recognise symptoms, take patients seriously and then to refer o
n of the physical signs and symptoms is necessary to make the complex symptomatology of ME/CFS understandable. He
port and criteria. He remarked that the various criteria tend to make this a diagnosis of exclusion, but it should be a prima
based on symptoms. He
he past scepticism and focus on this being a mental health issue – or even a figment of imagination! Doctors do need to s
believe in them. Identification of physical signs should support the symptom array to give diagnostic credibility as there a
as yet. All systems are affected.
nt on to discuss the physical signs, illustrated by a number of excellent photographs. Clinical signs are more evident in fe
discussed the fact that there are often "opposite" symptom types: lean v obese, hypermobile v stiff, hyponatraemic v hype
inted out that there is a subset with Ehlers Danlos Syndrome, and quoted the work of Dr Peter Rowe, but not all ME/CFS
mobility. Many of the photographs then shown were related to the hypermobility of joints throughout the body, skin char
, elasticity of skin and muscles, fingernail clubbing, difficulty maintaining posture etc.
ten a pre-phase of the disease – often these patients are "Duracell people" who are interested in everything and physically
search for hypermobility should be part of the evaluation
descending sympathetic tone pathway is abnormal, and vital functions are compromised during sleep. Normal "rescue ac
cur. When awake there are then haemodynamic problems – there has been no "rescue" by sleep, and symptoms (includin
sion) are then evident. Some increase in apnoea may also contribute to symptoms.

Carmen Scheibenbogen (Berlin, Germany) then spoke on auto-antibodies and acetylcholine receptors in ME/CFS. She e
tibodies directed against neurotransmitter receptors are causing various types of auto-immune diseases. 1/3 of patients in
gical outpatient clinic were found to possibly have ME/CFS. Immune activation (increased IgG levels, elevated ANA titre
ion) was found, leading to likely autoimmunity and disturbance of nervous system regulation. A role of auto-antibodies is
d, and treatment with rituximab may help after 3-4 months of treatment. This drug targets the auto-antibodies. Chronic str
auto-immune dysfunction. Japanese patients have also been found to have elevation of muscarinic acetylcholine antibodi
t auto-antibodies can activate immune cells by imitating adrenaline/acetylcholine stimulation. Various ME/CFS symptom
y overstimulation of the sympathetic/parasympathetic nervous system.Professor Scheibenbogen described the presence o
to molecules in the sympathetic nervous system.
sed the rituximab trials in Norway – some patients had improved and some had no response. Those patients improving had
on of the auto-antibodies, which then tended to stay low. Other treatments discussed included high dose immunoglobulin
sorption.

5 days. He uses “Microtacker” to look at mitochondrial mass (number). There are low mitochondria in naïve compared to
is also investigating T cell interactions with B cells, and is using an in vitro system looking at soluble factors released. Th
3 cell drugs, and much more research is needed.
from the audience asked if there was any legal way of getting rituximab. The answer was “No, we do not yet know enoug
tions”. Fluge and Mella do not want it used, because it is really their responsibility and their advice will be based on the la
underway at the moment in Norway. Doctors are advised not to treat with this drug outside a clinical trial at the moment.

Tom Wileman (East Anglia, UK) then discussed the gut virome in ME/CFS. The gut contains billions of bacteria, and ha
stem, which ignores our own bacteria, leading to homeostasis. It will attack “bad” bacteria. The immune system and micr
ance, but an inflammatory threshold may be reached leading to production of cytokines and interferons. This can then affe
ding to disease. Many diseases are implicated. A patient may have a predisposition because of host genes (immunophenot
o contains viruses, which are an important part of the inflammatory threshold. Some viruses live in or on the bacteria (pha
small and large viruses are involved. They may kill the good as well as bad bacteria. The virome and genotype compromis
enotype leading to an inflammatory threshold. The bacteria may then move into the immune system and upset the inflamn
The greater the diversity of viruses, the less the diversity of bacteria. The metabolites of bacteria maybe affected thus affec
stem.
need to find the viruses in the gut. The technique was explained with illustration. 100mg of faeces was placed in water, cer
d to obtain just the viruses. 16 samples of those with moderate ME/CFS have been studied. Each sample gives 2 million re
nen sequences the viruses. 23 different families of bacteria were found, each with different phages. The imbalance of phag
may correlate with disease. This has been shown in inflammatory bowel disease.

Don Staines (Gold Coast, Australia) gave an update from the NCNED (Griffith University) entitled “Receptor identificati
r signalling”. He described evidence for a channelopathy in B lymphocytes and Natural Killer (NK) cells. NK cell functio
ll in our body and this function can be measured in the laboratory to determine effectiveness of NK cells. In CFS/ME the
ave been shown by NCNED researchers and other groups to be significantly reduced in lysis function.
Receptor Potential ion channels (TRPs) may have a major role in the pathology of CFS/ME. These receptors are located or
he body. TRP receptors amplify activation signals, particularly via calcium, to impact gene regulation and other physiolog

cently published papers which reported examination of a large number of Single nucleotide polymorphisms (SNPs). At le
RP ion channel genes (TRPC4,TRPC2, TRPM3, and TRPM8) were identified to be significantly different in the ME/CFS
se SNPs were associated with TRPM3, while the remainder included TRPM8, TRPC2, and TRPC4 ($P<0.05$).
never been the identification of TRPM3 on NK cells or B cells prior to this study. NCNED researchers identified this rece
ne on NK cells and B cells in healthy people and importantly showed there was a significant reduction of TRPM3 receptor
nd B cells in CFS/ME patients.
e potential for a biomarker.
searchers also reported in both NK and B cells that had reduced TRPM3 receptors there was also a significant reduction in
r calcium levels as well as significant reduction in calcium stores in both NK and B cells. The presentation noted there w
changes in calcium pathways that are responsible for important cell functions. ERK 1 and 2, which are pivotal for NK cel
ficantly impaired, while a corresponding pathway to increase inflammatory pathways was significantly upregulated and m
natory cytokines that are reported in CFS/ME patients.
sion was that impaired TRP receptor function and impaired calcium signalling and stores are suggestive of the pathology

Simon Carding (Norwich Research Park, UK) talked about the work of the European ME Research Group (EMERG). He
addressing biomarkers, including brain imaging. Looking for cause, making a diagnosis and standardisation of samples sh
A “together approach” is needed. Euromene is a group of researchers hoping to establish a network across Europe. Eurom
ill work together. There is a need to look for opportunities for funding. They will build on current activity and feasibility,
is origin a) environment b) microbiome alterations
ical trials a) Rituximab b) Bacteria based therapy. Coming together is a beginning. Keeping together is progress
success. (Henry Ford) The Journal of Clinical Medicine has just accepted an article by Navena Navaneetharaja on: The R
Microbiota and Virome in ME/CFS. An audience question asked about role of probiotics: Answer: A cocktail of these is no
They may be helpful, but there is scant evidence.

Mady Hornig (Columbia, USA) discussed the programme at Columbia University. She pointed out that there are many m
rain disorders. There is also gastrointestinal comorbidity in brain conditions, including a subset with ME/CFS, and often s

oking at the balance of gut microbiota, too. Autoimmunity is modulated by intestinal microbes, so autoimmune responses
composition of the microflora in the gut. There is a mechanism described for a role for altered microbiota in the develop
immunity-associated eating and anorexic disorders, too.
istinct plasma immune signatures for ME/CFS present early in the course of the illness that differ from patterns observed
e illness. These phase-dependent immune patterns may have implications for how the disorder is treated of the course of i
so looking at the cytokine network analysis of the cerebrospinal fluid in ME/CFS.
y are trying to tie all this back to the microbiota. Regulation of the processes is critical - keeping things well balanced. So
on is necessary to protect against infectious illnesses, and also may be important in promoting key physiologic processes t
duction through the TCA cycle as well as brain processes (memory, cognition); however, inflammation that is uncontrolle
sting long after its initial trigger, has deleterious effects.
uch progress in our ongoing discovery of these mechanisms. A quote about Einstein probably sums up the progress:
from student: "The questions in this year's exam are the same as last year's!!" Einstein's reply, "Yes, but this year all the
it." The continuing burden of illness in ME/CFS demands that we recognize that new and more sensitive techniques must
ly be applied to be sure that we have not drawn premature and potentially incorrect assumptions about the pathogenesis of

Maureen Hanson (New York, USA) leads a large team looking at biomarkers for ME/CFS. She asked the question as to
narker. She provided 4 answers:
need for a diagnostic test to distinguish ME/CFS from other illnesses
need for objective measures for the effect of interventions and drug therapies
E - Research
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ction of participants for research
mation that can be used to identify underlying causes of ME/CFS and its major symptoms.
omarkers include:
ed NK cell activity
y cardio-pulmonary exercise tests
ormal brain imaging
biomarkers which need replication.
scussed the human microbiota – telling us that there are as many microbiota cells (mainly in the intestine) as human cells.
otection against pathogens. She cited an important issue of Science (April 2016) – "Microbiota at Work". Gut microbiota
ies are associated with disease (e.g. diabetes, Crohn's disease). The question is "Is this a cause or a consequence?" Assoc
ude diet, health status, genotype, age etc.
tinal symptoms are common in ME/CFS. Her lab's study of 38 female (30 controls) and 11 males (9 controls) was descril
fered intestinal discomfort compared to 8/39 controls.
eria have lipopolysaccharides on the surface and these can be a marker of inflammation when in the bloodstream. They are
y elevated in ME/CFS compared to healthy controls. sCD14 levels are also higher in ME/CFS. These findings indicate da
ey have also performed DNA sequencing of microbiomes. This can reveal the family and sometimes the genus. Operation
units are used to cluster the DNA sequences. A technique called Principal Component Analysis can be used to separate ar
pes of diets. However, this did not separate patients and controls, so other methods are needed.
iversity was looked at – the more sequencing, the more species are discovered. Controls show more diversity than patients
elp? Again the answer was that she did not know, and this needs further investigation.
oked at a computational method to identify ME/CFS from the blood and microbiome data. 83% of subjects, ill vs healthy,
lentified in this way. The limitations of these studies are:
the data are inadequate to identify particular strains of bacteria
do not reveal what beneficial pathogens are present
ndication of whether viruses are present
ese findings can be explained by psychological theories!

Elisa Oltra (Valencia, Spain) presented work on molecular biomarkers of ME/CFS. She said that biomarkers are needed
agnosis, and are essential tools for the development of effective treatments and preventive programs. She has chosen to w
s, which are stable molecules present in blood and other body fluids that can be easily implemented for monitoring diseas
ing and yet have been quite unexplored for the diagnosis of ME/CFS. Their association with disease relies in their functio
of gene expression by controlling target translation and/or degradation.
NA signature has been identified for the potential molecular diagnosis of fibromyalgia (FM). Genome-wide expression pro

, urine, saliva and stool at a cost per patient of $70,000. They have done a wide range of tests including 10 tests on sequer
ics and 7 immunology tests. He has the expertise and is developing new “devices” for molecular diagnostics. They are pa
more with metabolomics and services have been donated by “Metabolon”. The initial pilot data included 3 patients comp
ıtrols (precision medicine) and this was done on serum. This led to a massive amount of data. A lot of very big difference
een ME/CFS patients and healthy controls. He provided a list of the 24 largest metabolite outliers.
le, Tryptophan deficiency was present in one patient. This occurs because tryptophan is consumed during infection and af
ɔroduction. Melatonin controls sleep onset. Other examples discussed were biotin and BH4.
led by saying that it is common in research that responses are not always the same for mice and humans, and often mice a
ɔpment. For example, 150 drugs were shown to be effective in treating trauma in mice, but none of them worked in huma
really careful about requiring the use of mice for validating a drug.
ɜon wound up the conference with reference to the latest findings as discussed through the day. He took more questions a
points from the floor. He thanked the many talented speakers. The conclusion was that much exciting research is now for
as been a tremendous advance over even the past year, with much hope on the horizon.

k Invest in ME - Research and ANZMEs for making it possible for me to attend this very exciting day.