

MYALGIC ENCEPHALOMYELITIS (ME): SCIENCE, MEDICINE & POLITICS

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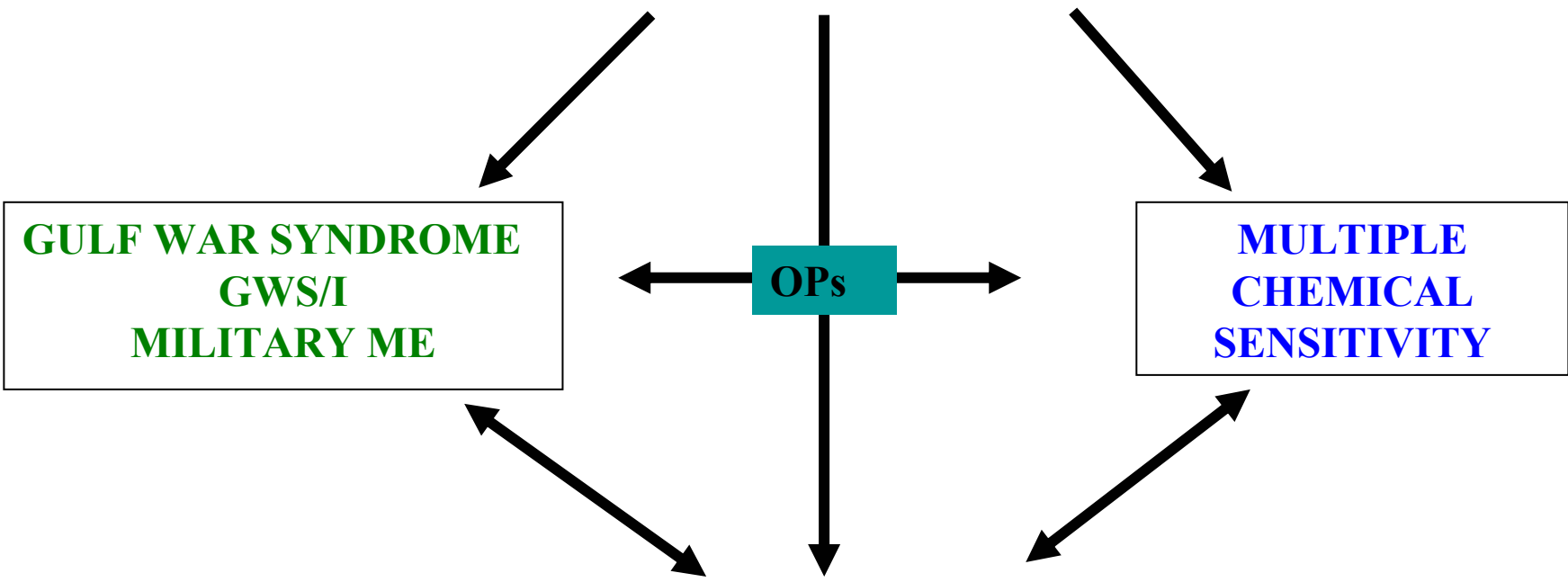
Stockholm Lectures 2nd October 2007

Medicinal Chemistry – fairly recent discipline that concerns the design and development of novel drugs (including pesticides, herbicides, etc)) for the treatment any disease.

Involves knowledge of chemistry, biochemistry, pharmacology, vaccines, microbiology, some aspects of medicine.

HOW DID IT ALL START?

SYNDROMES OF UNCERTAIN ORIGINS
Merck Manual 1999, 17th Edition



GULF WAR SYNDROME
GWS/I
MILITARY ME

MULTIPLE
CHEMICAL
SENSITIVITY

ME-CFS
FMS

OPs

COMPLEX MULTI-SYSTEM &
MULTI-ORGAN ILLNESSES
NEUROLOGICAL- ANS, PNS, CNS
CARDIOVASCULAR
IMMUNE SYSTEM
GASTROINTESTINAL
RESPIRATORY
ENDOCRINE SYSTEM

“Considering the extent of the patients’
complaints and disability, the results of
ROUTINE laboratory tests were
strikingly **NORMAL**” S Straus

SOMATISATION- PSYCHIATRIC- THEY ARE ALL IN THE MIND

WHAT'S IN A NAME? ME vs CFS

**WHO - ICD 10 - G93.3 (FROM 1969) IS CLEAR
MYALGIC ENCEPHALOMYELITIS IS A NEUROLOGICAL DISORDER
MUSCLE PAIN WITH INFLAMMATION OF THE BRAIN AND SPINAL
CORD**

**[THE ONLY ALLOWED ALTERNATIVE NAMES ARE
POST-VIRAL FATIGUE SYNDROME, PVFS, CHRONIC FATIGUE SYNDROME, CFS]**

**ME DESCRIBES A PATHOPHYSIOLOGICAL CONDITION WITH CLEAR MEANING
FOR CLINICIANS AND ALLIED SCIENTISTS**

PVFS DESCRIBES AETIOLOGY (VIRUS INDUCED) + A SYMPTOM - FATIGUE

**CHRONIC FATIGUE DESCRIBES A SYMPTOM – SUBJECTIVE – PROVIDES NO
CLINICAL SIGNS FOR DIAGNOSIS- MAKES MISCHIEF POSSIBLE**

NOT ENCEPHALOPATHY (TOO VAGUE BUT ENCEPHALOMYELITIS)

WHY CFS ?

FIRST AGREED IN 1988 AT AACFS – A DIVISIVE VOTE.

Prof Anton Komaroff (2007) “None of the participants in creating the 1988 CFS case definition and name ever expressed any concern that it might TRIVIALISE the illness. We were insensitive to that possibility and WE WERE WRONG.”

CURRENTLY CFS IS WIDELY USE BUT IN RESPONSE TO PATIENTS CONCERNS CFS-ME OR ME-CFS IS ALSO COMMON.

THE NAME IS A CONTINUALLY DEBATED AND DISPUTED BY DOCTORS, PATIENT GROUPS, ACTIVISTS, RESEARCH WORKERS & CONCERNED PARLIAMENTARIANS.

OPPOSED BECAUSE IT IS USED TO IMPOSE PSYCHIATRIC MODELS OF THE ILLNESS AND DIRECT INEFFECTIVE AND INAPPROPRIATE TREATMENT. CREATES CONFUSION IN SELECTING PATIENTS FOR RESEARCH STUDIES.

IS THIS A BATTLE WE NEED TO FIGHT ? IS IT TOO LATE TO CHANGE?

THE DECEPTION !

FATIGUE SYNDROMES ARE CLASSIFIED IN ICD-10 AT F48.0
MENTAL & BEHAVIOURAL DISORDERS

MYALGIC ENCEPHALOMYELITIS – CHRONIC FATIGUE SYNDROME
[NEUROLOGICAL DISORDERS]



~~CHRONIC~~

~~SYNDROME~~

FATIGUE SYNDROMES – [MENTAL & BEHAVIOURAL DISORDERS]

NEUROLOGY
G93.3



PSYCHIATRY/PSYCHOLOGY
F48.0

ME CLASSIFICATION AND NOMENCLATURE

ME is

NOT a Fatigue Syndrome classified under ICD-10 F.48.0 Mental and Behavioural Conditions

PROPOSED ICD-10 6TH REVISION –F.48.0 Mental & Behavioural includes Neurasthenia / Fatigue Syndrome EXPRESSLY EXCLUDES ME-CFS

NOT Chronic Fatigue - many causes, Amer Med Assoc 1990

NOT Burnout/ – cortisol responses differ Mommersteeg et al

NOT DECONDITIONING - Burnett.

NOT Clinical Depression fails clinical tests – eg. blood flow in the brain – Richardson, Hyde, Carruthers. A study from Harvard, 1990, was unable to correlate an immunologic abnormality with the degree of depression.

THE CASE FOR INFLAMMATION - ENCEPHALOMYELITIS

- 1. PATHOLOGY**
- 2. INFLAMMATION AND OXIDATIVE STRESS
PHYSIOLOGY/BIOCHEMISTRY**
- 3. INTERFERONS – PKR – NITRIC OXIDE – RNaseL**
- 4. GENETICS**

DR ABHIJIT CHOUDHURI – CONSULTANT NEUROLOGIST, OLD CHURCH HOSPITAL, ROMFORD ESSEX



Examined post mortem tissue from a number of people who died with ME. What did he find

1. Classical markers for severe inflammation of sections of the spinal cord - dorsal root ganglia where sensory nerves enter the spine.

2. The nature of these markers varied with the length of the illness

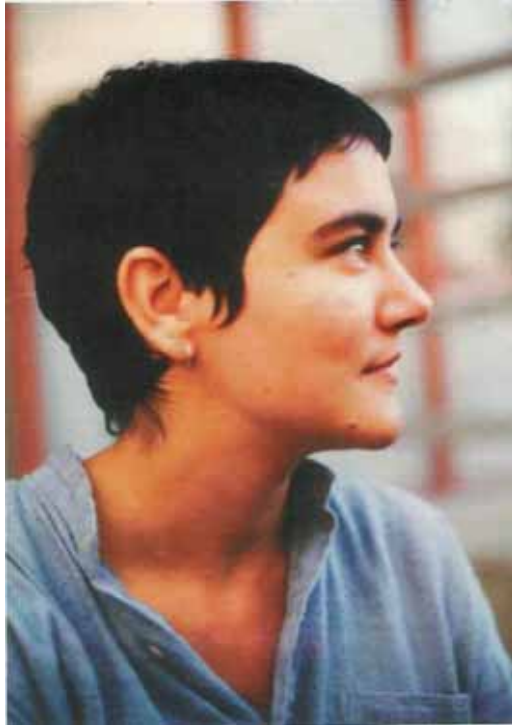
After 20 years corpora malacea were identified man of 32. This is only found >40 years except in Down's syndrome.

After 6 years (F. 26) inflamed active cytotoxic T lymphocytes

3. Take home message - the markers for the illness change with the time of the illness.

4. Establishing tissue banks would be useful; Petersen – Whitemore Institute

“PATHOLOGY DOES NOT LIE” - INFLAMMATION OF SPINE = MYELITIS



SOPHIA MIRZA

POST MORTEM FOUND EXTENSIVE (75%) INFLAMMATION OF DORSAL ROOT GANGLIA (SENSORY INPUT) OF THE SPINE CONSISTENT WITH A MAJOR VIRAL INFECTION

<http://www.investinme.org/International%20ME%20Conference%202007%20-%20DVD%20Orders.htm>

**The
INTERNATIONAL
ME/CFS
CONFERENCE 2007**

***Energising ME
Awareness***

Clinical Diagnosis, Treatments,
Support and Research of
Myalgic Encephalomyelitis

CPD Accredited Conference

Organised by the charity INVEST in ME
Charity Nr. 1114035

Abhijit's lecture is included in this set of DVDs of the Invest in ME London Conference May 2/3 2007

A similar lecture was also given in Adelaide in March 2007

Sophia's story was part of the 2006 conference and is available at

<http://www.investinme.org/Article-050%20Sophia%20Mirza%2001.htm>

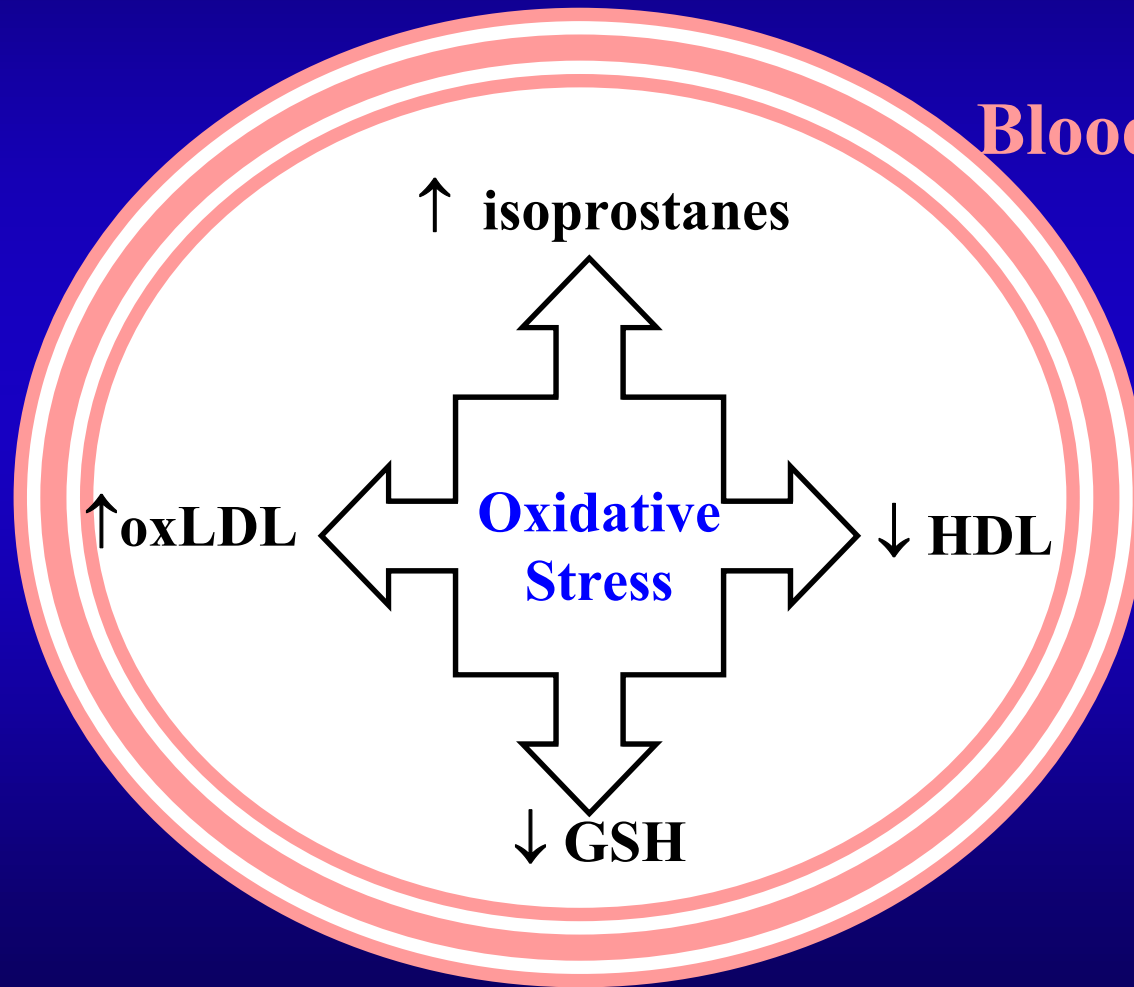
**Oxidative stress levels are raised in chronic fatigue
syndrome and
are associated with clinical symptoms**

**Gwen Kennedy*, Vance A. Spence, Margaret McLaren,
Alexander Hill,
Christine Underwood, Jill J.F. Belch**

Free Radical Biology & Medicine 39 (2005) 584 – 589.

Markers of Oxidative Stress

0



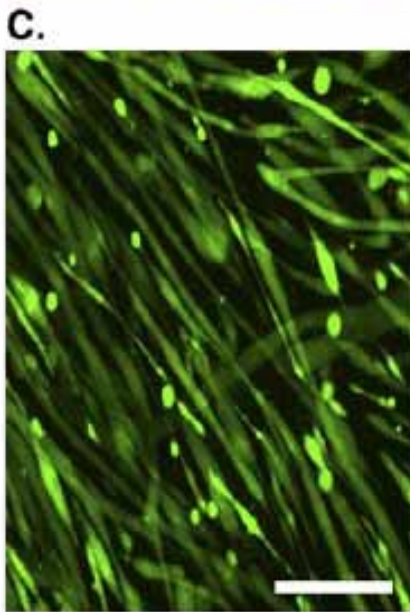
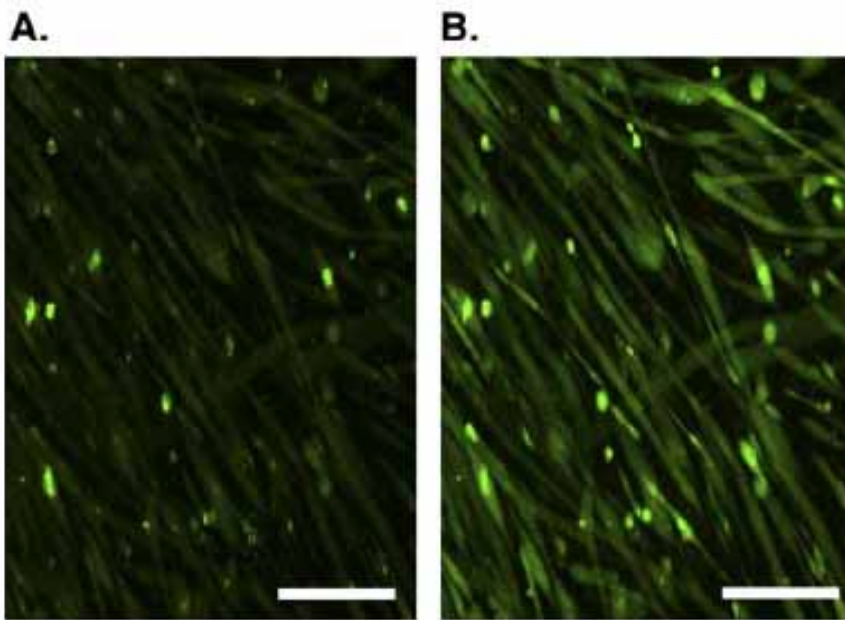
Blood vessel wall

Results

	HDL (mMmol/L)	OxLDL (mU/mL)	GSH (μ mol/L)	Isoprostanes (pg/mL)
CFS/ME patients	1.32 (0.34)**	39.8 (13.9)#	1258 (260)*	462 (245)##
CFS/ME controls	1.63 (0.46)	32.3 (10.9)	1370 (233)	332 (118)
<hr/>				
OP patients	1.20 (0.26)~	35.8 (17.1)	1260 (299)	397(146)
OP controls	1.46 (0.45)	35.0 (11.9)	1275 (183)	339 (118)
<hr/>				
GW patients	1.06 (0.20)	32.2 (12.0)	1209 (187)	367 (125)
GW controls	1.22 (0.34)	34.2 (9.0)	1236 (211)	309 (106)

Mean (SD) Unpaired t-test patients vs controls

***p=0.05, ~p=0.025, #=p=0.02, **p=0.001, ##p=0.005**

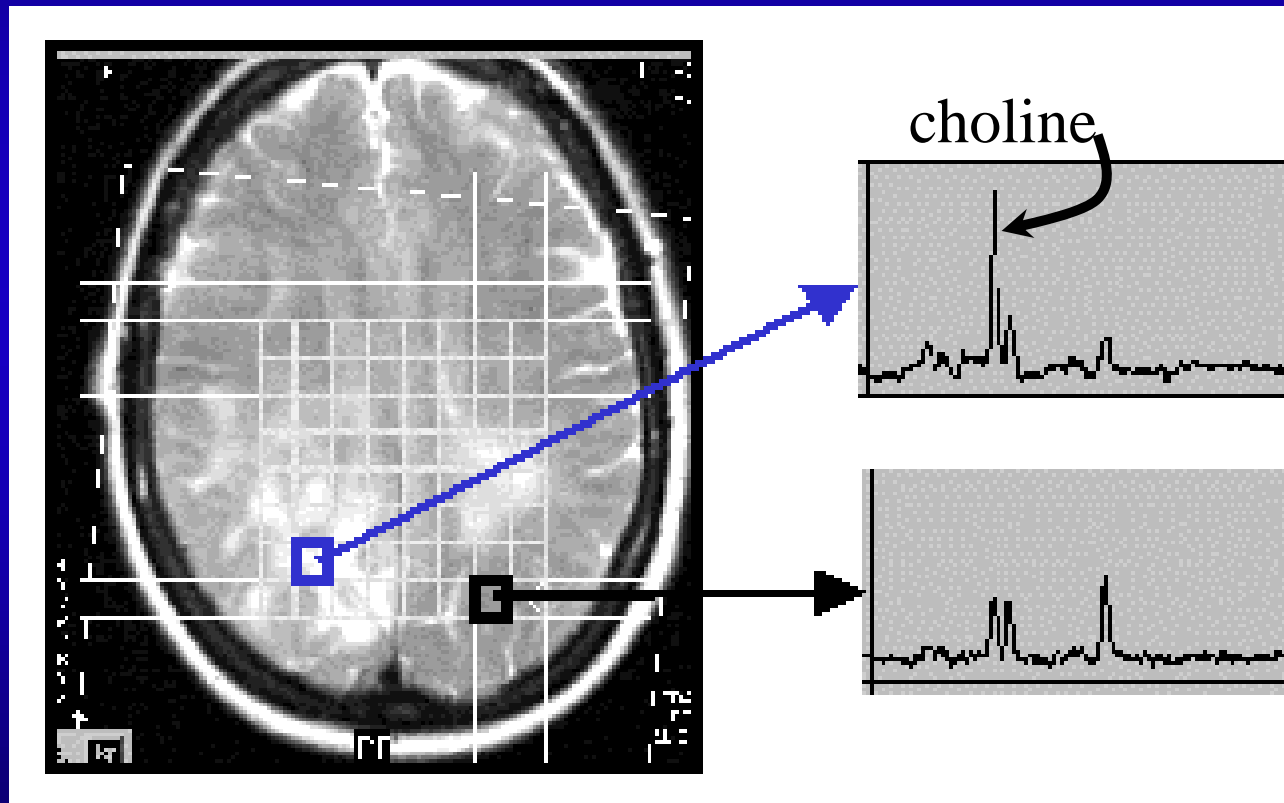


McArdle et al FRBM 2005;39:651-7
Showing free radical (reactive oxygen species) increasing with exercise.

Erythrocyte Oxidative Damage in Chronic Fatigue Syndrome
Ross S. Richards, Lexin Wang and Herbert Jelinek
Archives of Medical Research 38 (2007) 94-98

Fig. 2. Images of DCF fluorescence from myotubes after 10 min at rest (A) 10 min of contractile activity (B), and following a further 10 min at rest (C) Bar = 100 μ m.

MR Spectroscopy showing increased choline/creatine ratio



Chaudhuri A, Condon BR, Gow JW, Brennan D, Hadley M. Brain Imaging 2003;14:225-8.

Chaudhuri A, Behan PO. In vivo magnetic resonance spectroscopy in chronic fatigue syndrome. Prostaglandins Leukot Essent Fatty Acids. 2004;71:181-3

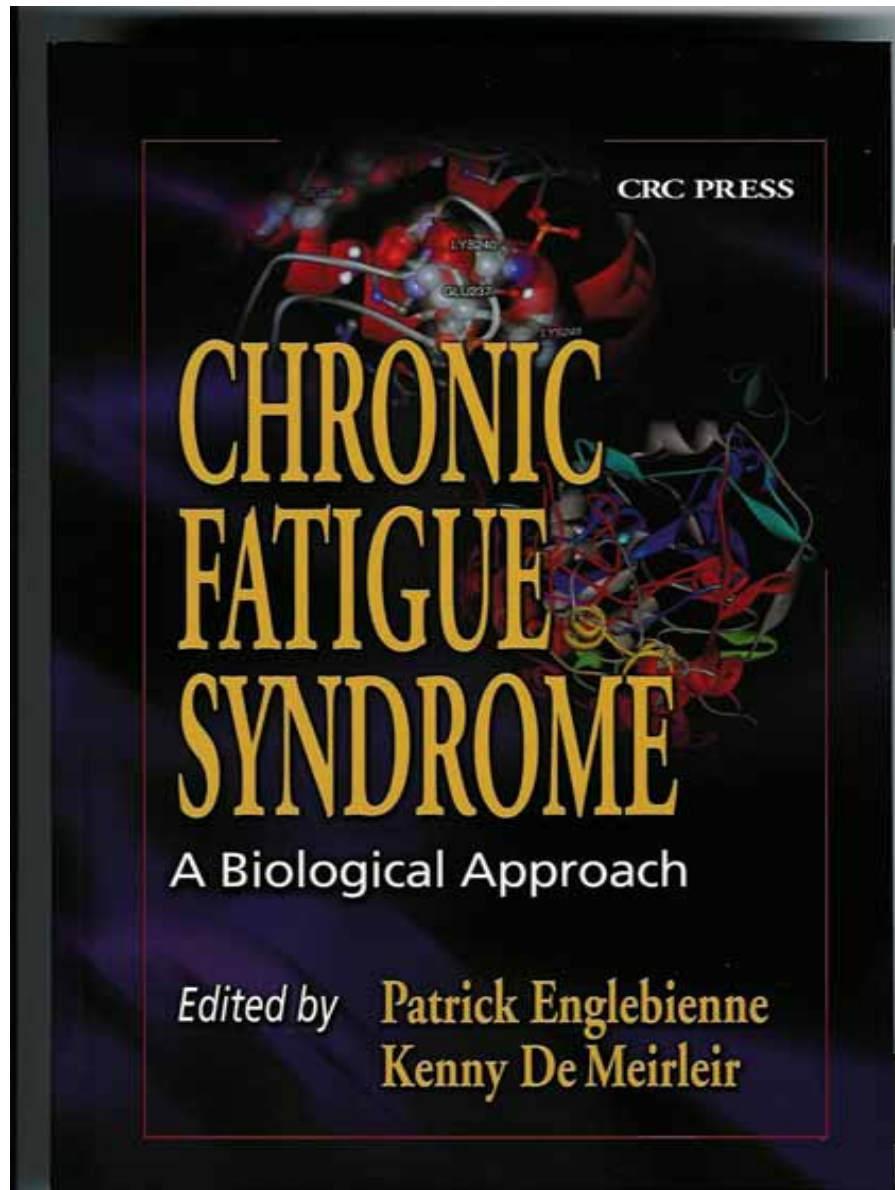
Basant Puri et al Acta Psychiatr Scand 2002;106:224-6

Using MRS found Choline /creatine ratio was significantly higher in ME patients with loss of normal spatial distribution of Choline than controls.

**Abnormal phospholipid metabolism in brain in CFS –
CONSISTENT WITH INFECTION AND INFLAMMATION**

PUFAs have a major role in membrane stability and function. Important for the effective functioning of embedded structures, enzymes, receptors, ion channels etc

EXTENSIVE IMMUNOLOGICAL DISRUPTION IN M.E.



**An in-depth
consideration of the
disordered PKR & 2-5A
RNA Synthetase
pathways underlying
persistent, aberrant
responses to
intracellular viral &
other microbial
infections underlying
ME/CFS**

**CRC Press 2002 ISBN 0-
8493-1046-6**

ORIGINAL ARTICLE

Gene expression in peripheral blood mononuclear cells from patients with chronic fatigue syndrome

N Kaushik, D Fear, S C M Richards, C R McDermott, E F Nuwaysir, P Kellam, T J Harrison, R J Wilkinson, D A J Tyrrell, S T Holgate, J R Kerr

16 genes differentially expressed (15 up- 1 down- regulated in patients vs. controls

Involvement of genes from several disparate pathways suggests a complex pathogenesis.

1. T-CELL ACTIVATION (IMMUNOLOGY)- JR COXSACCHIE – ANNE CUNNINGHAM TO UNPACK

2. NEURONAL (ICD-10 G.93.3)

3. MITOCHONDRIAL (SARAH MYHILL - HANDOUT)

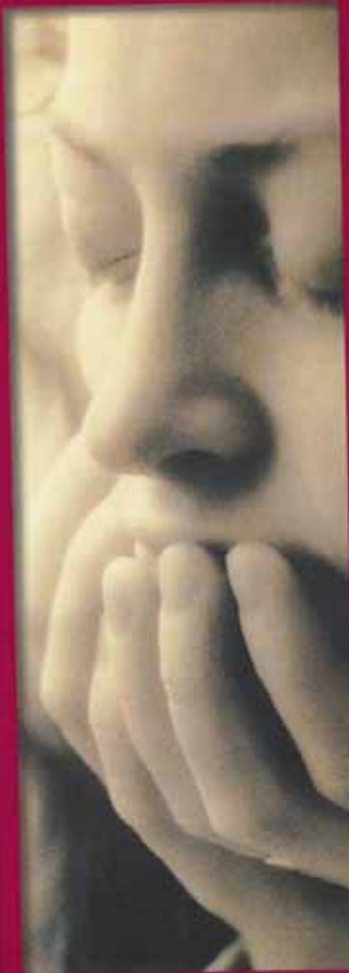
ABNORMALITIES

NTE GENE CONSISTENT WITH LINKS WITH OP POISONING- RCEP



**CHRONIC
FATIGUE
SYNDROME,
GENES, and
INFECTION**

*The Eta-1/Op
Paradigm*



Early T-cell activation

Bone - Handling phosphate and bone and calcium metabolism – joints , tendons

Cardiovascular effects including endothelium function and cell migration, calcification.

Liver necrosis.

Skin.

Kidney.

Lung.

GIT.

Nervous system.

Reproductive system.

Auditory System.

Neoplasia

Haworth Press 2003

ROBERTO PATARCA-MONTERO, MD, PHD



MAJOR CHAPTERS ON VIRUSES

Cardiovascular Consequences

Central Nervous System

Glandular Effects

Pregnancy

Neoplasms

Toxins OCs mimic ME

Treatment Considerations

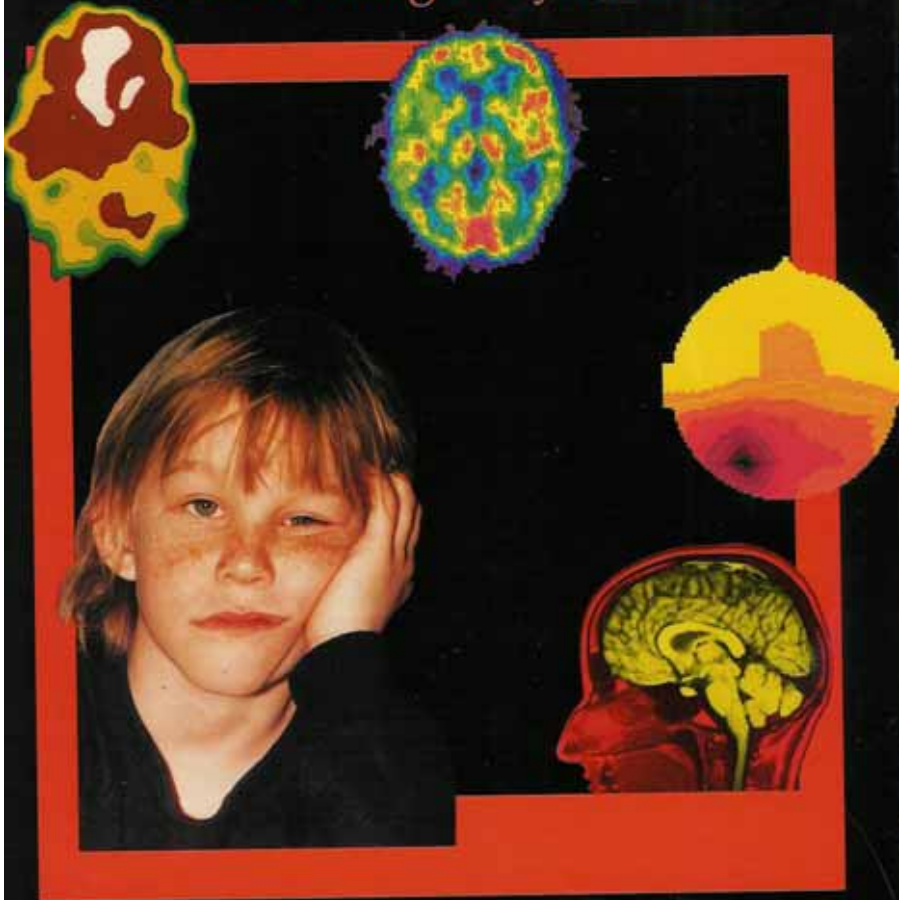
**THIS IS A MAJOR CLINICAL
WORK THAT REPRESENTS A
LIFE TIME OF DEDICATED STUDY
AND PATIENT CARE.**

**Brain blood flow by PET Scans
differentiates ME/CFS from depression**

ISBN 0-7890-1127 Haworth Medical Press, 2001

Byron Marshall Hyde, M.D.

The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome



The Nightingale Research Foundation

**1992- Byron Hyde, Jay
Goldstein, Paul Levine
(Eds)**

**74 Chapters covering all
aspects of ME-CFS**

**Modern Techniques- SPECT,
PET, MRI (MRS)**

Numerous Clinical Studies

Multi system effects

Effective Treatments

M. Kroger

**Myalgic Encephalomyelitis/
Chronic Fatigue Syndrome:**

**A Clinical Case Definition
and Guidelines for
Medical Practitioners**

**An Overview of the Canadian
Consensus Document**

Bruce M. Carruthers
Marjorie I. van de Sande



DIAGNOSIS/DEFINITION

Numerous Schemes

LONDON

OXFORD

FUKUDA (Research)

ALL UNSATISFACTORY

Limited or no consideration of
organic disease/illness

**MANY MISSED DIAGNOSES –
NO NEED TO INVESTIGATE!**

Experienced clinicians and
Scientists from Canada, USA,
and Europe with 1000s of
hours of clinical cases.

Consulted widely and reached
A CONSENSUS.

1994 Case Definition: CDC Fukuda et al Ann Int Med Dec 1994

Characterised by:

Medically unexplained
Of new onset
At least 6 months duration
Not the result of ongoing exertion
Not substantially relieved by rest
Substantial reduction in previous activities

OBLIGES ALL RESEARCH WORKERS TO USE CFS NOT ME IN RESEARCH & PUBLICATIONS

FUKUDA and EARLIER DEFINITIONS NOT ADEQUATE AND IGNORE VITAL RESEARCH STUDIES – Spence et al Ann Epidemiol 2004;14:95-100

Four of the following:
impaired memory/concentration
Sore throat
Tender cervical lymph nodes
Myalgia
Headaches of new type
Unrefreshing sleep
Post-exertional malaise
Multi joint pain without swelling or redness

CANADIAN CONSENSUS PANEL CRITERIA FOR M.E. - 2003

MAJOR COMMON FEATURES

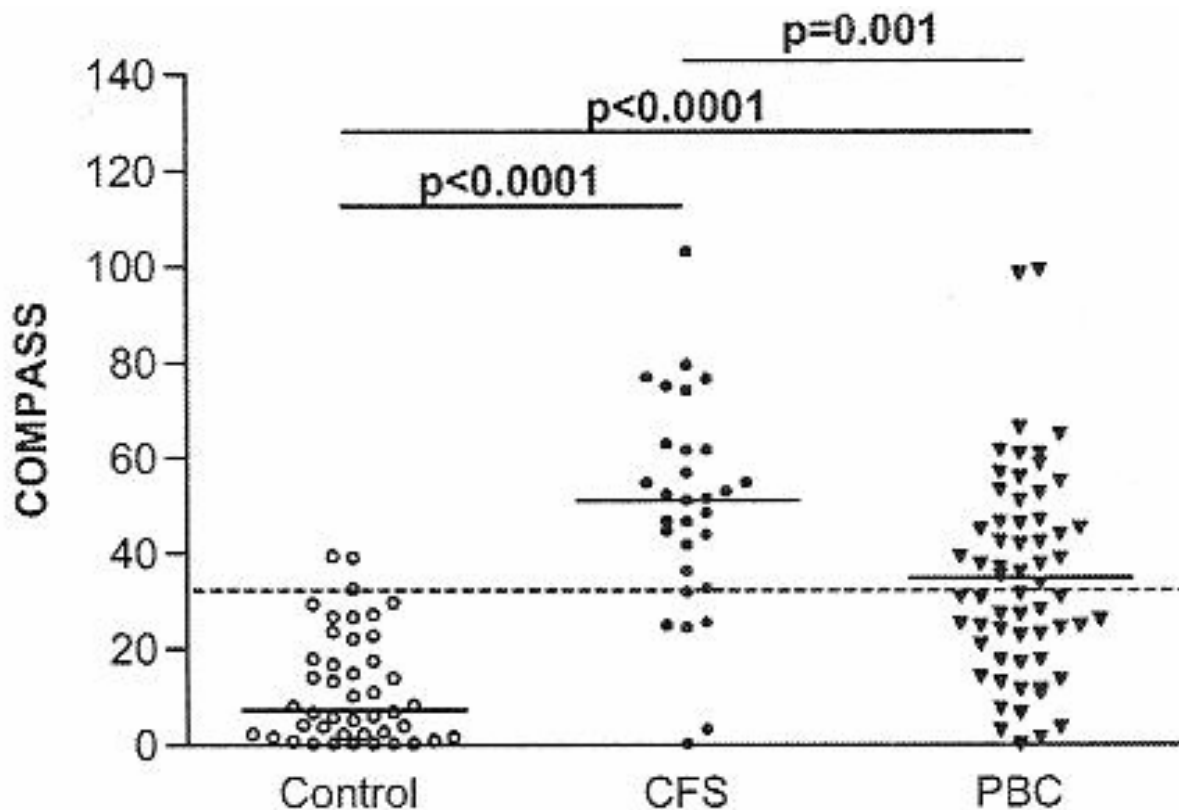
- **FATIGUE**
- **POST-EXERTIONAL MALAISE & FATIGUE**
- **SLEEP DISORDERS**
- **PAIN**
- **NEUROLOGICAL /COGNITIVE MANIFESTATIONS (2 or more)**

AT LEAST ONE SYMPTOM FROM 2 OF FOLLOWING CATEGORIES

AUTONOMIC - NMH, POTS, Delayed Postural Hypotension, Low plasma and/or RBC volume, Vertigo, Light Headedness, Extreme pallor, Intestinal or Bladder, disturbances with IBS or Bladder dysfunction, Cardiac Arrhythmias, Vasomotor Instability, Respiratory Irregularities

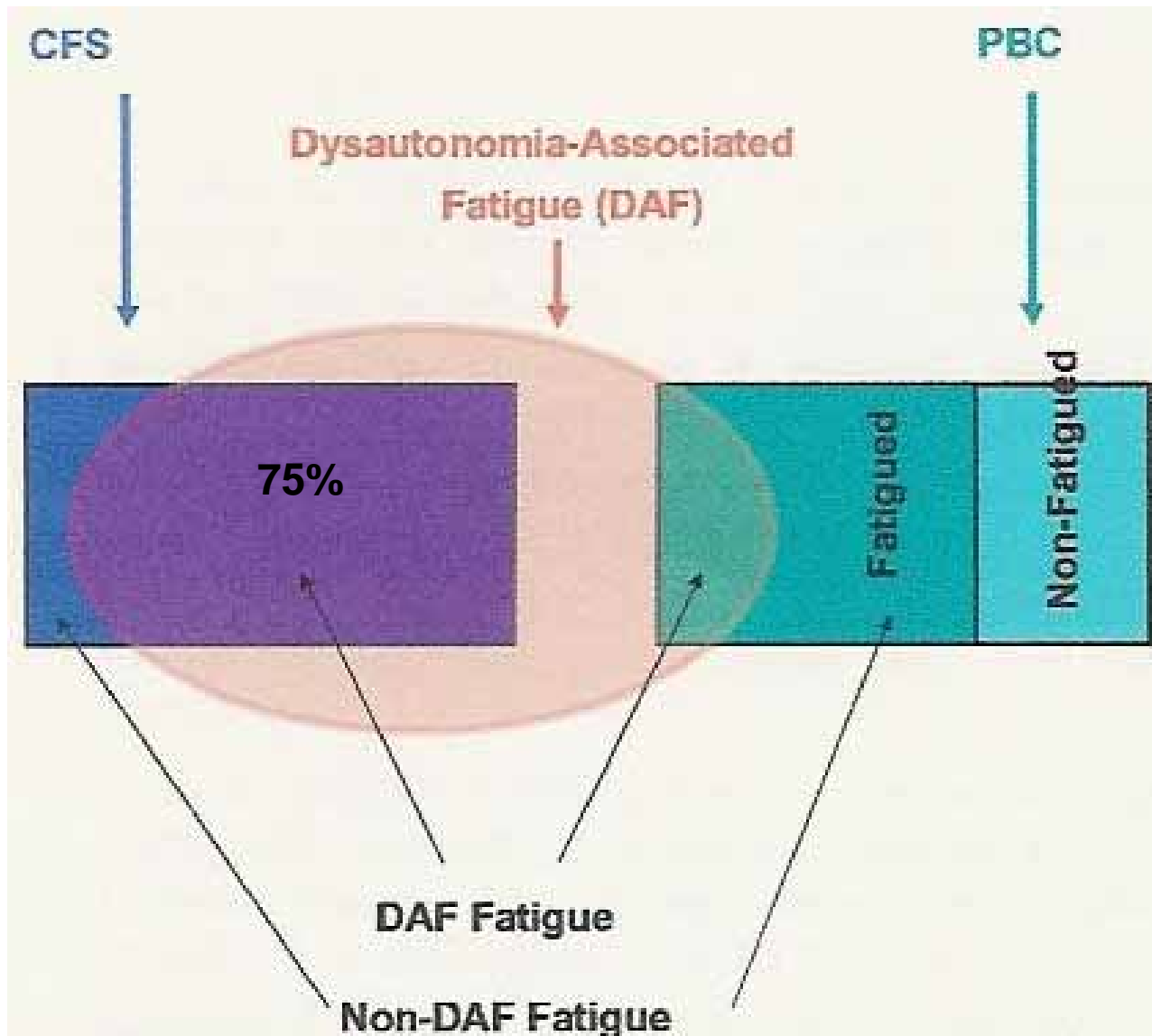
NEUROENDOCRINE - Thermostatic instability- heat/cold intolerance, Anorexia or Abnormal Appetite, Marked weight change, hypoglycaemia, loss of adaptability /tolerance to stress and slow recovery from stress, emotional lability

IMMUNE - tender lymph nodes, sore throat, flu-like symptoms, general, general malaise, development of new allergies or change in status of old ones, hypersensitivity to medications and/or chemicals.



COMPASS –8 DOMAIN GLOBAL SCALE FOR AUTONOMIC DYSFUNCTION

In particular there were strong correlations between HRV and OT, Over all there was no significant association with a psychosomatic scale, fatigue vs understatement scale. No significant relationship with length of history and COMPASS scores indicating that deconditioning was not an explanation of the fatigue.



**NEED FOR
SUBGROUPS**

**NOT ALL ME-
CFS PATIENTS
HAVE
DYSAUTONOMIA**

Roberto Patarca-Montero. JCFS 2000:7(4):1 “the sorting of patients into subpopulations....is helping in the design and interpretation of clinical trials for therapeutic interventions aimed at particular disease manifestations”.

Chronic Fatigue Syndrome: The Need for Subtypes

**Leonard A. Jason,^{1,4} Karina Corradi,¹ Susan Torres-Harding,¹
Renee R. Taylor,² and Caroline King³**

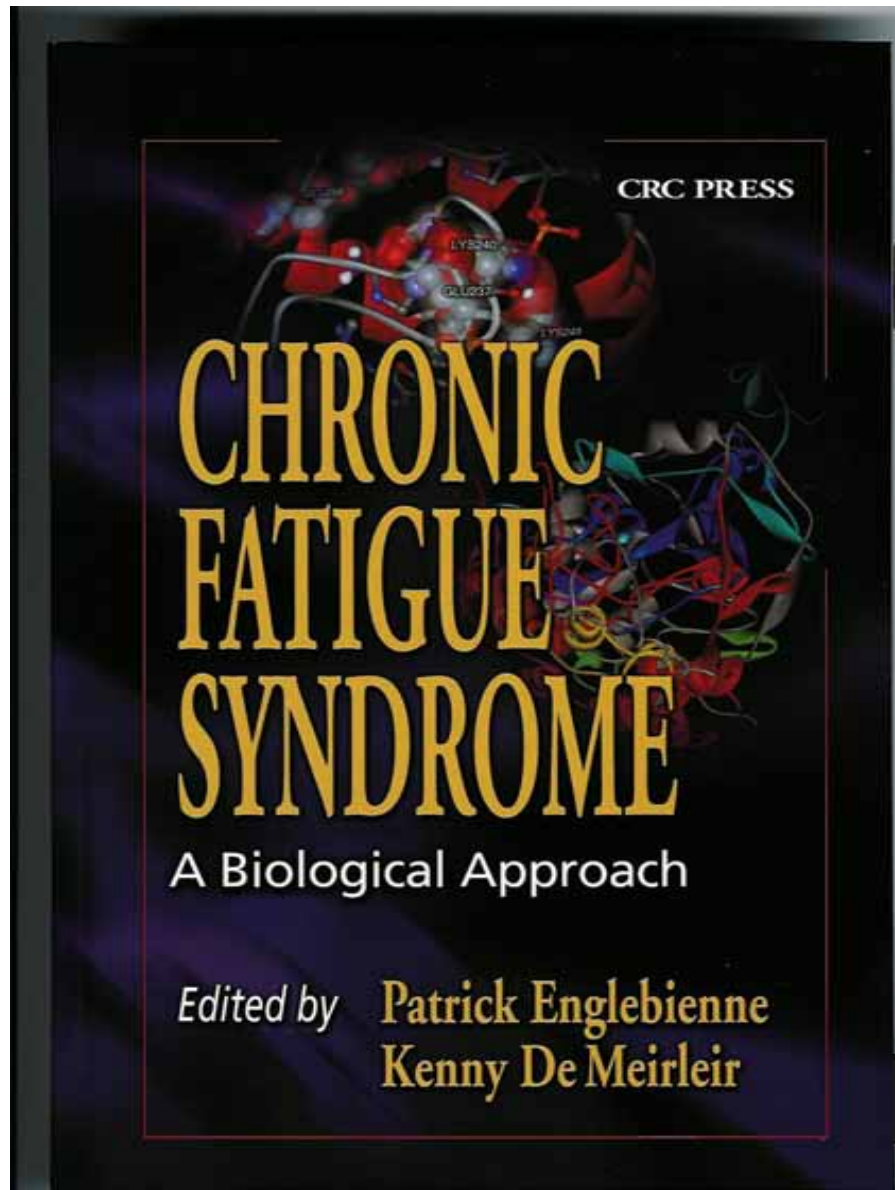
**CFS-ME vs. CFS/ME with PSYCHIATRIC COMORBIDITY –MAJOR DEPRESSIVE DISORDER
CURRENT CDC 1994 DEFINITION INADEQUATE – CANADIAN BETTER.**

NEUROCOGNITIVE FUNCTIONING MANY NEARLY NORMAL IN SOME TESTS- SF-36.

SOCIODEMOGRAPHIC – LOWER RATING MORE DISABILITY

**MEDICAL – VIROLOGY – IMMUNOLOGY- NEUROENDOCRINOLOGY – ANS- NEUROLOGY –
GENETICS- TREATMENTS. CBT – ZERO AFTER 3 YRS**

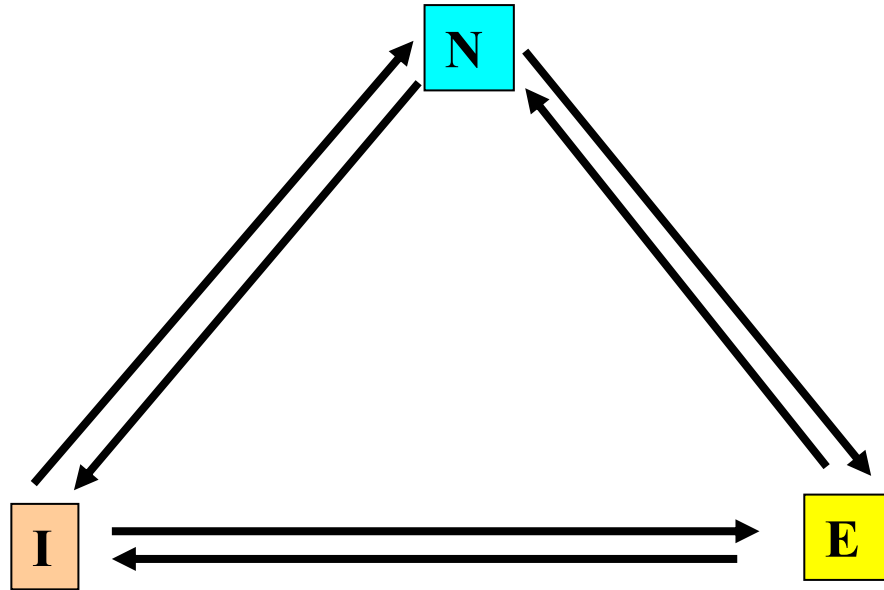
A COMMON IMMUNOLOGICAL MECHANISM FOR M.E.



**An in-depth
consideration of the
disordered PKR & 2-5A
RNA Synthetase
pathways underlying
persistent, aberrant
responses to
intracellular viral & other
microbial infections
underlying ME/CFS**

**CRC Press 2002 ISBN 0-
8493-1046-6**

NEUROENDOCRINEIMMUNE PARADIGM (NEI) PSYCHONEUROIMMUNE (PNI)



MANY OF THE MESSENGER MOLECULES INVOLVED IN THE BRAIN AND NERVOUS SYSTEM ARE ALSO INVOLVED IN THE IMMUNE AND ENDOCRINE SYSTEMS AND VICE VERSA DISTURBANCE OF ONE SYSTEM WILL OFTEN LEAD TO DISTURBANCES IN ANOTHER

DIESEL EXHAUST FUMES ALTER THE TH1/TH2 BALANCE IN THE SAME WAY AS ALLERGIES Senechal et al Am J Respir Crit Care Med 2003;168:215-221

Engelbienne, De
Meirleir et al.

MULTIPLE TRIGGERS



**COMMON PATHWAY ACTIVATED –
RNaseL + PKR**



MULTIPLE BIOLOGICAL MECHANISMS

**OXIDATIVE STRESS; NO·, ROS, RNS, etc
DYSREGULATION OF PROSTAGLANDIN
METABOLISM – VASOCONSTRICTION & PLATELET
AGGREGATION REDUCED ACTIVITY OF NK CELLS
- HPA DEPRESSED CRH DOWN.**

Ca⁺⁺ DYREGULATION – Sk/HEART MUSCLE

APOPTOSIS; TH1 → TH2 SHIFT

Spence et al J ClinPath 2004;57:891-3

M.E. CAN THEREFORE BE DEFINED AS AN ILLNESS ASSOCIATED WITH AN ABERRANT IMMUNE RESPONSE THAT PERSISTS AND INDUCES A PROLONGED INFLAMMATORY RESPONSE AFFECTING THE CNS PROVOKING A RANGE OF DISTRESSING BIOLOGICAL EFFECTS

TRIGGERS

INTRACELLULAR MICRO-ORGANISMS

- 1. VIRUSES - RETROVIRUSES – HERVs, HIV, PICORNAVIRUSES - ENTEROVIRUSES, VACCINIA, etc. –Richardson, Chia**
- 2. CHLAMIDIAE, RICKETTSIAE, BORELLIA, MYCOPLASMAS, TB. – Hyde, Kerr**
- 3. VACCINES- Meningococcal B (Norway), BCG, Hep B others. Pirot, Kerr, Hyde**

CHEMICALS

- 1. PESTICIDES - OPs, [GWS], Cl₅phenol, Kerr et al., De Meirleir**
- 2. HERBICIDES - GLYPHOSATE, GLUFOSINATE - Kerr**
- 3. SOLVENTS - methyl tert-butyl ketone, benzene at ppb! – Vodjani et al**
- 4. HEAVY METALS – Pb, Hg, Zn ((xs), Cr, Cd, Ni, As. De Meirleir et al**

**Chia JKS. The Role of Enteroviruses in Chronic Fatigue Syndrome-
A Review J Clin Pathol 2005;58:1126-32**

Enteroviruses are well known causes of acute respiratory and gastrointestinal infections, with tropism for the central nervous system, muscles and heart. Initial reports of chronic enteroviral infections causing debilitating symptoms in patients with CFS were met with skepticism, and largely forgotten for the past decade.....Recent evidence not only confirmed the earlier studies but also clarified the pathological role of viral RNA through antiviral treatment.

Ribavirin, interferon- α , pleconaril [JR –pooled immunoglobulins early, choline + ascorbic acid.]

Probable cause	No. of patients (<i>n</i> = 200)
Enterovirus infection Persistent	109
Unknown —	44
<i>Chlamydia pneumoniae</i>	18
Epstein-Barr	6
Cytomegalovirus infection	3
Recurrent VZV infection Recurrent lesions;	6
Recurrent HHV6-like disease	1
Parvovirus B19 infection	3
Hepatitis C	3

ORIGINAL ARTICLE

Chronic fatigue syndrome is associated with chronic enterovirus infection of the stomach

John K S Chia, Andrew Y Chia

J Clin Pathol. 2007 Sep 13; [Epub ahead of print]

Kenny De Meirleir - Group 1: (15 to 20 percent)

High levels of LMW RNase L and elastase, low levels of protein kinase (PKR) and uric acid, and low to normal levels of nitric oxide. Elevated levels of lymphocytes and proteins in the spinal fluid, increased pressure upon opening the lumbar puncture

Chronic low-grade viral infection and inflammatory reaction in the brain. Many micro-organisms are associated with this profile. Heavy metals, pesticides, and other triggers may also be involved. ~ 20 percent have low-grade Herpes Virus 6A (HHV6A) encephalitis. [cf Chia]

Neurocognitive problems – confusion, impaired concentration and memory. Fatigue originates in the brain. Pain is not prominent. Some similarities to (MS).

Group 2: (10 to 15 percent)

Very high levels of LMW RNase L and elastase, high protein kinase activity, severely low natural killer cell activity, and very low serum uric acid levels.

Severely ill - bacterial infections originating from animals such as pets, rodents, ticks, etc.

Severe bowel problems. 70 % of immune cells are in the digestive tract. Leaky gut syndrome, increase in gut permeability - foreign proteins enter the blood and tissues and inflammation results. Tests for 12 pathogenic gut bacteria.

Group 3: (60 to 70 percent)

Majority of ME/CFS patients in this group. Profile similar to Group 2, but not as severe. Generalized pain originating from dysfunction in the pain processing areas of the brain and CNS is a prominent feature. GI infections with bacteria in the blood.

BIOMARKERS

1. Get patient to stand still for 5- 10 minutes [tilt test]
2. MRI -diffuse vasculitis in brain, Hyde.
3. hsCRP (much used for CV disease!- see Myhill)– Spence et al
4. RNaseL – De Meirleir et al
5. Blood proteins allied to genetics studies – Kerr et al

TREATMENTS

1. **CBT (Cognitive Behavioural Therapy) & GET (Graded Exercise Therapy)**
aka somatisation, biopsychosocial approach
antidepressants.
2. **ANTIVIRAL TREATMENTS**
3. **OTHER ANTIMICROBIAL TREATMENTS**
4. **IMMUNOMODULATION**
5. **MITOCHONDRIAL SUPPORT**
6. **OTHER COMPLEMENTARY THERAPIES**
Essential fatty acids,
7. **Other therapies**

FUNCTIONAL SOMATIC SYNDROMES: ONE OR MANY?

Wessely et al Lancet 1999;354:936-9

Gastroenterology – IBS, Non-ulcer dyspepsia

Gynaecology – PMS, chronic pelvic pain

Rheumatology – Fibromyalgia

Cardiology – Atypical or non-cardiac pain

Respiratory medicine – hyperventilation

Infectious Disease – PVFS- ME-CFS

Neurology – Tension headache

Dentistry – TMJ dysfunction, Atypical facial pain

ENT – Globus syndrome

ALLERGY - MCS

**CANNOT EXPLAIN
BY CONVENTIONAL
PARADIGMS**

**CONVENTIONAL
THERAPY INEFFECTIVE**

**MORE COMMON IN
WOMEN THAN MEN**

**SHARE NON-SPECIFIC
SYMPTOMS**

**CLAIMS ALL THESE SYNDROMES RESPOND TO SAME THERAPIES,
CBT/GET, OFTEN WITH ANTIDEPRESSANTS**

SOMATIC MEDICINE ABUSES PSYCHIATRY – AND NEGLECTS CAUSES

An almost TOTAL lack of SCIENTIFIC support

Reclassifying BODILY symptoms as MENTAL problems...where CONVENTIONAL medicine is at a loss for an explanation.

LACK OF firm KNOWLEDGE is converted into SPECULATIVE ASSERTIONS without any CRITICAL voices being heard. PD, MS, Diabetes

Causal explanation for illnesses .. go with predominantly somatic symptoms [that] lack any basic similarity to known mental disorders.

An evasive argument...with its lamentably poor record of research into causes, particularly where environmental factors are concerned.

Industrial interests are actively influencing the course of what is ostensibly a scientific discussion.

What makes an individual human being ill cannot be determined by statistics

Lack of knowledge is a considerable handicap in the treatment of chronic diseases

Per Dalen (Psychiatrist) http://art-bin.com/art/dalen_en.html

Mercury, Lyme's disease, placebo effect, toxicology, epidemiology

N McLaren THE BIOPSYCHOSOCIAL MODEL and FRAUD

This model is based on fraud and ignorance and a complete misunderstanding of the origins of the idea. It is a myth.

“I see psychiatry under attack from all quarters. Some people see a great future for us. I don’t share that view. I believe there is a serious risk that psychiatry as we know it will no longer exist in as little as fifteen years. The reason is simply a lack of anything approximating an adequate intellectual framework for our efforts.”

The myth of the biopsychosocial model.

Australian and New Zealand Journal of Psychiatry 2006; 40 (3), 277-278

<http://www.futurepsychiatry.com/> Chapters 7 and 9

This model was the basis for the rejection of the Class Action brought by GWVs and persists still- see Phil Trans Royal Soc 2006;631:689-695.

Carruthers BM Definitions and aetiology of myalgic encephalomyelitis how the Canadian consensus clinical definition of encephalomyelitis works. J Clin Path 2007;60:1170119.

The widespread use of the holistic biopsychosocial model of disease without distinction between a clinical entity and its background encourages “drowning” of clinical entities by risk factors which can proliferate endlessly in a nominalist fury without orientation as to their state of relevance or lack thereof with respect to a real entity.

Nominalism (phil) doctrine that universal or abstract terms are merely names. Concise Oxford Dictionary

MUPS, PUPS, MUS with regard to GWVs.

In writing the history of a disease, every philosophical hypothesis whatsoever, that has previously occupied the mind of the author, should lie in abeyance. This being done, the clear and natural phenomena of the disease should be noted - and these only. They should be noted accurately, and in all their minuteness.

Sydenham 1676 and subsequent editions Classics of Medicine

“to arrange reality to save it can cause much error”

MISREPRESENTATION AND WORSE

**FITNESS FOR WORK - OUP-2004 REPRINT £50-00 IN ASSOCIATION WITH
RCP FACULTY OF OCCUPATIONAL MEDICINE**

WESSELY et al p.132 - incl, Maurice LIPSEGE Consultant Psychiatrist KCL.

BRIEF INFECTION (USUALLY VIRAL) >>>

VULNERABLE PERFECTIONIST PERSONALITY + PRESSURE AT WORK

EMPLOYEE SICKNESS ABSENCES>>>

FATIGUE >>>>

PROLONGED BED REST >>>>

MALADAPTIVE BELIEFS >>>

CHRONIC INVALIDISM>>>

TERMINATION OF SERVICE ON MEDICAL GROUNDS.

ALL LAZY CHILDREN - INACTIVE >>>>

+/- PENSION !

STEPHEN RALPH -12/6/04 - www.meactionuk.org.uk

THE BATTLE CONTINUES !

Psychoneuroendocrinology 2005;30:990-5

Biological sensitisation and psychological amplification: Gateways to subjective health complaints and somatoform disorders

Ingvard Wilhelmsen*

The theory is supported by recent research and may result in better handling of patients ...

DO NOT LISTEN TO YOUR OWN BODY'S SIGNALS

DO NOT TRUST YOUR FEELINGS

DO NOT TRUST YOUR THOUGHTS

CURRENT CLINICS STILL WEIGHTED TOWARDS PSYCHIATRIC THEORIES AND PACING, CBT, GET WITH PSYCHIATRISTS IN CHARGE AT MENTAL HOSPITALS.

Dr M Sharpe Edinburgh International Science Festival, April 10th 2004

“Groups should be as mixed as possible – no definition”

**“we widened the terms of referral in order to ENHANCE RECRUITMENT”
Inclusion/Exclusion Criteria MRC trial of Pacing, CBT, GET. (White & Wesseley)**

Dr A Pinching

Did not accept that evidence existed to justify treating different sub-groups of patients differently...more appropriateto respond to their individual needs under the BROAD umbrella term (CFS?)

**“Our worries about names, causation, mechanisms which OK are FUN
....can be understood by others as a reason for inaction....over investigation can be harmful.....causing them to seek abnormal test results to validate their illness”**

“over-investigation can be harmful and counter-productive to the management of these patients, causing them to seek abnormal test results to validate their illness” [ROUTINE TESTS NORMAL]

“patients avoid activity but then develop symptoms of deconditioning or excessive awareness of physiological changes” [NOT DECONDITIONING]

VIRUSES – ANTIVIRAL AGENTS

POOLED Human IgG (IM,IV)- ADOLESCENTS (RICHARDSON et al, Ben Nathan)

ANTIVIRALS -VALGANCYCLOVIR (HERPES FAMILY),

PLECONARIL - picornaviruses, enteroviruses, rhinoviruses etc

INTERFERONS (β - KERR),

AMPLIGEN etc (DER MEIRLEIR)

LAURICIDIN

OLIVE LEAF EXTRACT



Demographic and clinical data on twelve patients with long-standing fatigue and central nervous system dysfunction who received valganciclovir therapy

Patient #	Age	Gender	Flu-like onset	Duration of illness (years)	% of pre-illness activity level		Months on treatment
					At baseline	After treatment	
Responding patients							
1	57	M	Yes	7.5	25	95	6
2	21	M	Yes	7	5	90	6
3	14	F	Yes	1.5	15	90	6
4	48	F	Yes	3.5	15	95	6
5	46	M	Yes	2.5	15	90	6
6	24	F	Yes	1	5	70	6
7	27	F	Yes	1	5	85	6
8	42	F	Yes	8	10	80	3
9	33	F	Yes	1	10	80	6
<i>Median values for responders</i>	33	F	Yes	2.5	10*	90*	6
Non-responding patients							
1	52	F	No	15	25	25	3
2	49	F	No	3	25	25	2
3	28	F	Yes	<1	10	10	3
<i>Median values for non-responders</i>	49	F	No		25	25	3

*p < p=0.007.

900mg bid for 3 weeks followed by 900 mg daily to complete 6 months treatment

OTHER ORGANISMS-

CHLAMYDIA, CHLAMYDOPHILA, RICKETTSIA, BORELIA, MYCOPLASMA

DOXYCYCLINE, CLARITHROMYCIN, MINOCYCLINE, AZITHROMYCIN, QUINOLONES(CIPROFLOXACIN etc), CHLORAMPHENICOL. Prolonged – 6 weeks- and repeat cycles (2-6) with spacing to check on evidence of infection.

ESSENTIAL TO SUPPORT GENERAL HEALTH AND ESPECIALLY TO PROTECT THE GUT-

PRO- & PRE-BIOTICS

VITAMINS/MINERAL SUPPLEMENTS

GUT ENZYMES

GLUTAMINE

Nicolson CFIDS Chronicle September/October 1999.

Dr Sarah Myhill MB BS, Upper Weston, Llangunllo, Knighton, Powys, Wales, UK LD7 1SL
Tel: 01547550331 Fax: 01547550339 E-mail: smyhill@globalnet.co.uk Website: www.drmyhill.co.uk

Dictated July 2005

I think this is one of the most important handouts I have ever produced in terms of my understanding of CFS and what to do in order to recover! So please read this very carefully and several times over because for many sufferers it contains the keys to unlock their illness!

CFS IS HEART FAILURE SECONDARY TO MITOCHONDRIAL MALFUNCTION

Am J Med Sci 2003;326:55-60

Abnormal Impedance Cardiography Predicts Symptom Severity in Chronic Fatigue Syndrome

ARNOLD PECKERMAN, PHD; JOHN J. LAMANCA, PHD; KRISTINA A. DAHL, MD;
RAHUL CHEMITIGANTI, MD; BUSHRA QUREISHI, MD; BENJAMIN H. NATELSON, MD

Sinatra Solution- Metabolic Cardiology. Stephen T Sinatra – Amazon Books

**VARIOUS REPORTS AND STUDIES HAVE FOUND THAT
SOME SUPPLEMENTS ARE HELPFUL**

NADH, SUCCINATE, CoQ 10

Dr Sarah Myhill BSAENM – www.drmyhill.co.uk

ME/CFS is low grade heart failure arising from mitochondrial dysfunction

Support mitochondrial functions – CoQ10 300-360 mg daily, L-carnitine 2000-3000 mg daily, D-Ribose – 15 grams divided daily, Magnesium 400-800mg daily after SINATRA

Coupled with MMMs – Se, Zn, Mo etc

**General vitamin supplement, Sarah also uses high dose 1-5mg daily of B12- many find this helpful. Free radical scavenger. [Chandy]
Vit C, carotenoids, Vit E part of natural antioxidant cascade**

Other antioxidants include lycopene, pycnogenols, etc

CONFUSION AND DECEPTION AROUND CASE DEFINITION BEDEVILS

**PATIENT CARE & UNDERSTANDING,
CARERS AND THEIR NEEDS,
SUPPORT SYSTEMS BENEFITS, INSURANCE,
CLINICAL TREATMENT AND RESEARCH STUDIES.**

**SEVERELY AFFECTED ME (MYALGIC
ENCEPHALOMYELITIS) ANALYSIS REPORT ON
QUESTIONNAIRE ISSUED JANUARY 2004**

Analysis Report by

25% ME Group

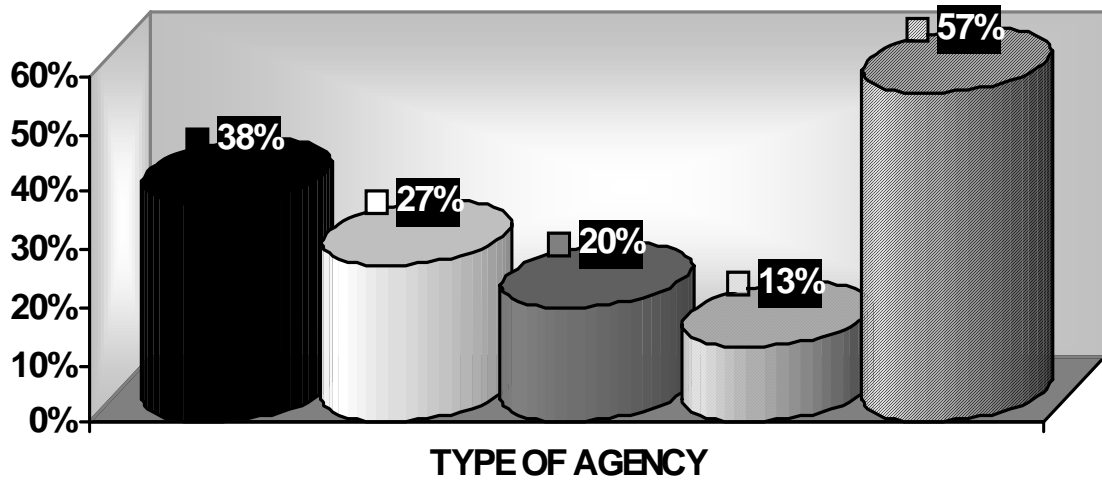
1st March 2004

<http://www.25megroup.org/>



Google Search

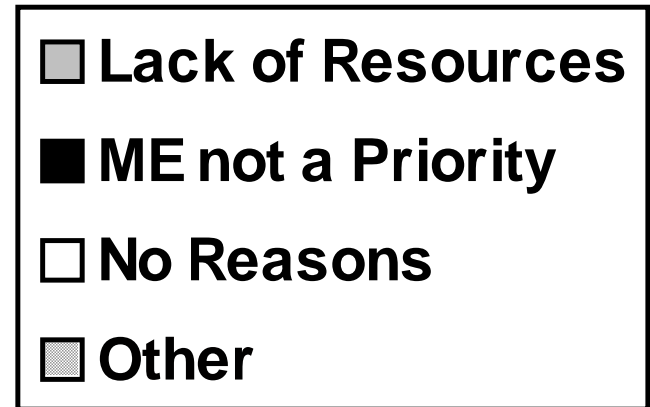
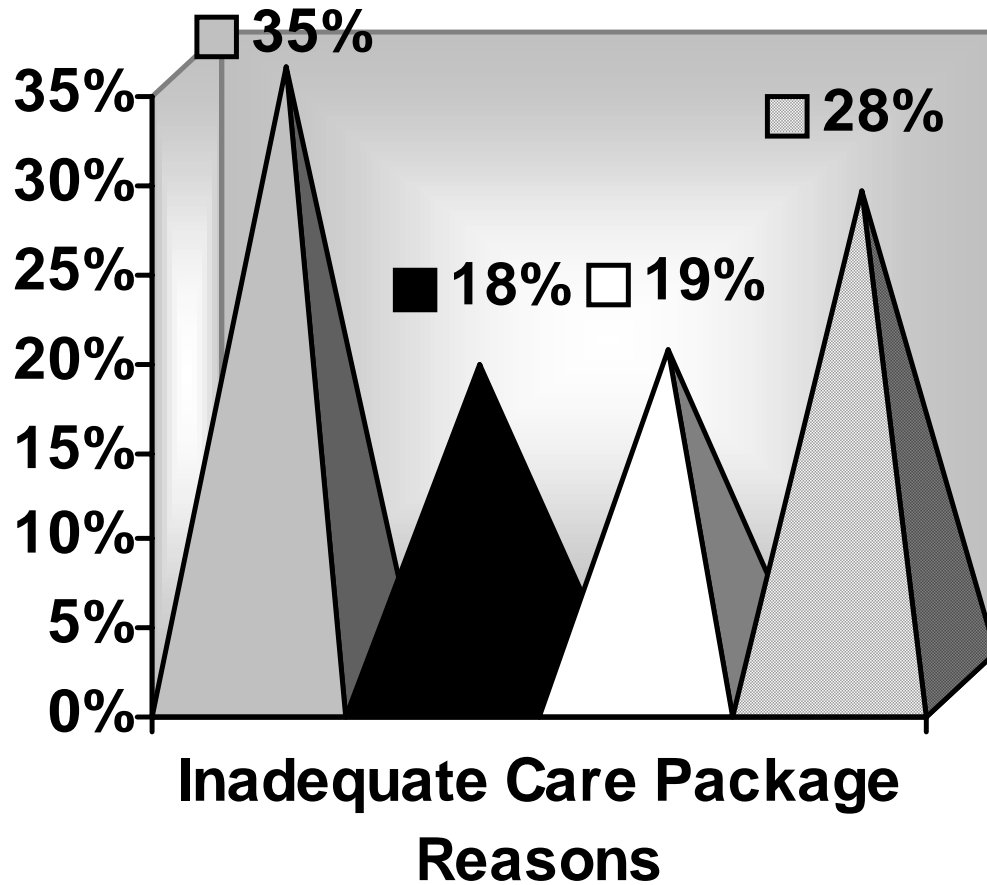
AGENCIES REGARDED AS ACCEPTING ME AS A LONG-TERM SERIOUS ILLNESS



COMMUNITY CARE

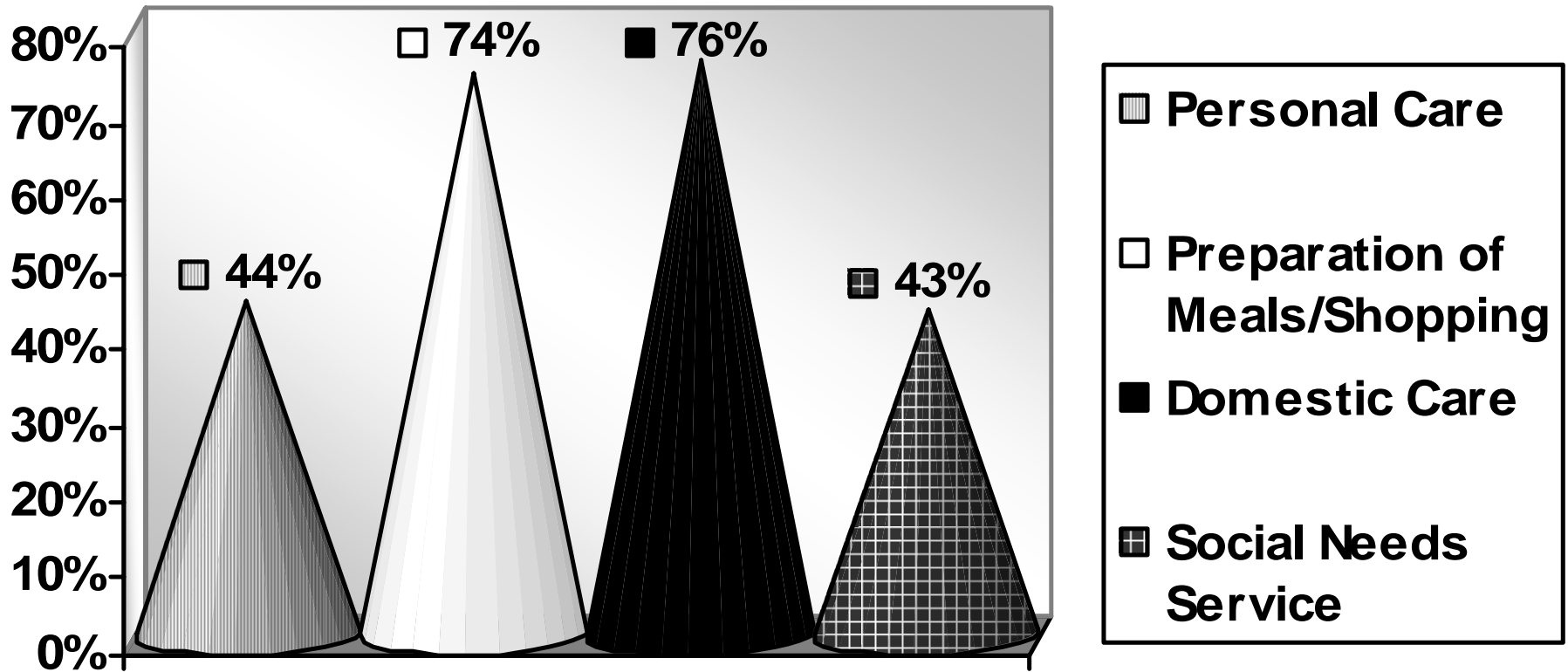
COMMUNITY CARE ASSESSMENT	YES/ O	NOS.	%
HAVE A SOCIAL WORKER/CARE MANAGER	YES	127	29%
	NO	310	71%
HAVE HAD COMMUNITY CARE ASSESSMENT	YES	195	45%
	NO	242	55%
ADEQUATE CARE PACKAGE RECEIVED	YES	77	39%
	NO	118	61%

**61% FELT CARE
PACKAGE
INADEQUATE**



Several people reported ONLY receiving an adequate care package following an appeal and A HIGH COURT JUDGEMENT IN CLAIMANTS FAVOUR!.

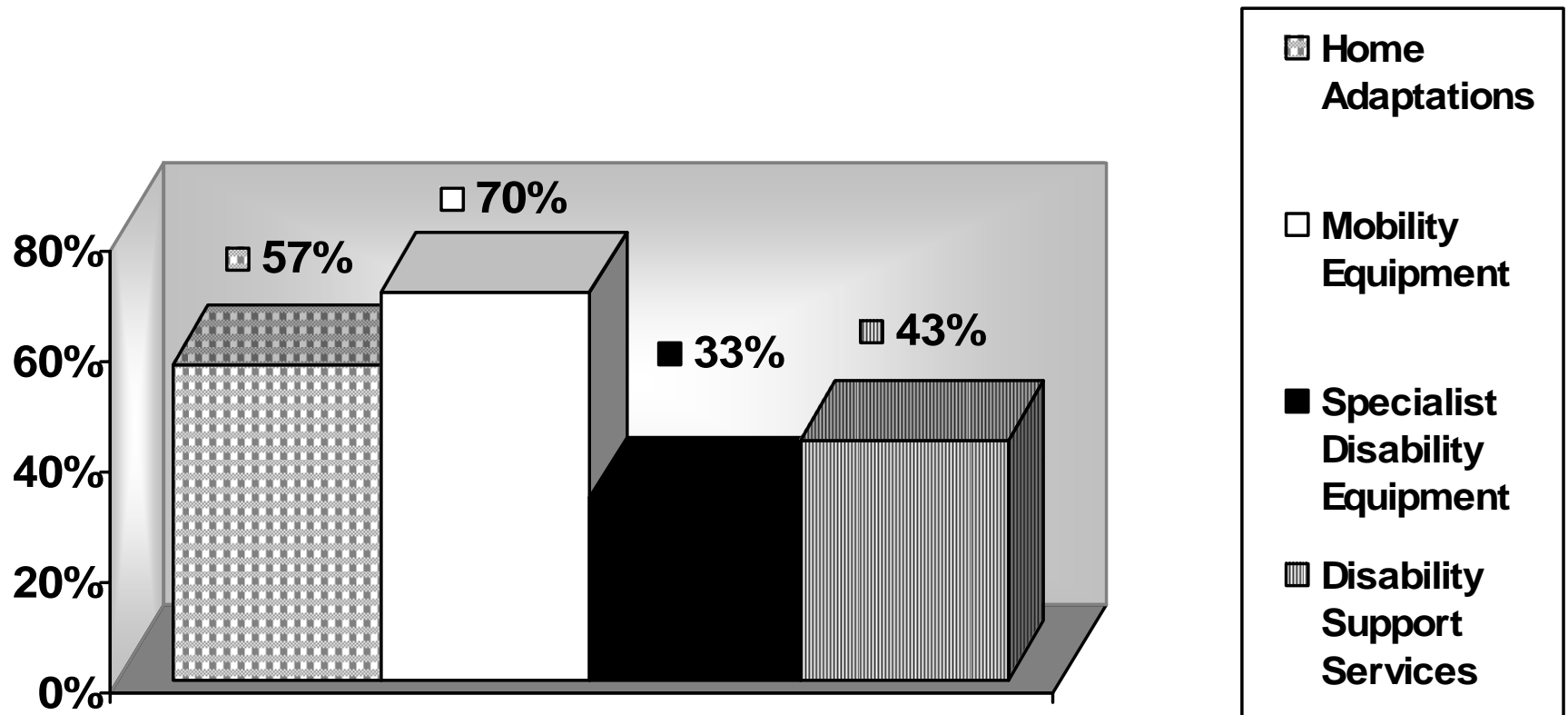
PERSONAL CARE



OCCUPATIONAL THERAPY ASSESSMENT

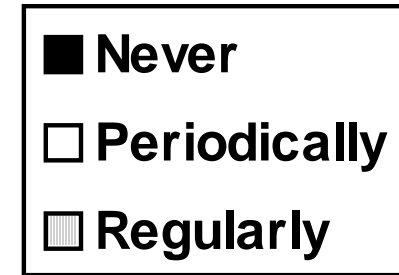
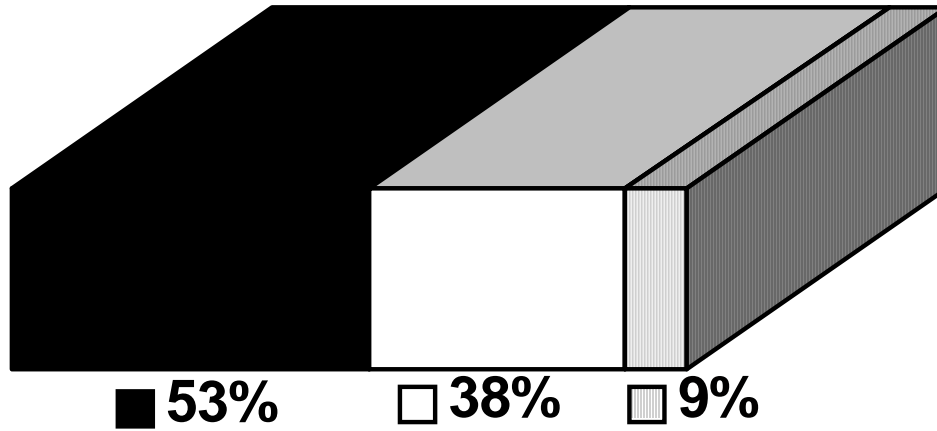
OCCUPATIONAL THERAPY ASSESSMENT (OTA)	YES/NO	NOS.	%
HAVE HAD OT ASSESSMENT CARRIED OUT	YES	223	51%
	NO	214	49%
OTA FULFILLED DISABILITY REQUIREMENTS	YES	118	53%
	NO	105	47%
WAITED OVER 6 MONTHS FOR OT ASSESSMENT	YES	93	42%
	NO	130	58%

DISABILITY AIDS REQUIREMENTS



**ONLY 20% OF CARERS HAD HAD THEIR NEEDS ASSESSED
87% DID NOT FEEL VALUED BY SOCIETY**

GP HOME VISITS



25% ME GROUP [THE SEVERELY AFFECTED-1/3/O4

RANDOM SAMPLE -437 = 66% OF MEMBERSHIP

COMMENTS ON TREATMENTS GIVEN

	H%	UNH%
PERSON-CENTRED COUNSELLING	54	46
PSYCHOTHERAPY	10	90
CBT*	7	93
GET*	5	95
PACING*	70	30
ALTERNATIVE THERAPIES	60	40
SYMPTOMATIC CARE MANAG	73	30
PAIN MANAGEMENT	75	25

*** SO WHY HAS £8.2 MILLION BEEN COMMITTED TO CLINICS OFFERING ONLY THESE TREATMENTS?**

Statement from Solihull & Birmingham M.E. Support Group

Assurances given that the new ME/CFS services would operate independently from the psychiatric service. THIS IS NOT THE CASE.

Appointment letters headed

**“THE BIRMINGHAM AND SOLIHULL MENTAL HEALTH TRUST” WHOSE ADDRESS IS
QUEEN ELIZABETH**

ALL MEETINGS OF THE ME/CFS STRATEGY GROUP HELD WITHIN THE LOCKED QEPH

**“Accordingly the ME Support Group has advised their patient representative TO
DISENGAGE FROM FURTHER PARTICIPATION OR DIALOGUE UNTIL ... SUCH TIME AS
THE GROUP IS SATISFIED THAT SUCH ASSURANCES HAVE BEEN GIVEN”.**

**STOP PRESS – THE DWP IS TO REVISE ITS PROCEDURES AND REGULATIONS HAVING
RECOGNISED THE SERIOUS NATURE OF ME/CFS AS AN ORGANIC ILLNESS**

**SOUTH OF TYNE CFS SERVICE 28TH JUNE 2006-
SERVICE PLANNING PROCESS**

**“the Service WOULD OPERATE FROM AND BE BASED ON THE
BIOPSYCHOSOCIAL FRAMEWORK””**

Dr Tony Wells- Clinical Consultant Psychologist

**ALL THE LOCAL/REGIONAL GROUPS INVOLVED IN THE PLANNING PROCESS
HAD REJECTED THE BPS MODEL FOR THE SERVICE.**

**BUT IT WAS STATED ON THE DAY THAT IT WOULD STILL BE THE BASIS OF THE
SERVICE.**

THIS FRAMEWORK WAS REJECTED ON THE DAY! BY THE LOCAL GROUPS

**THIS IS DECEPTION AND IMPOSITION OF A PRE-PLANNED SERVICE WITHOUT
LISTENING TO THE VOICE OF THOSE MOST INVOLVED.**



New Horizons

International Conference on
ME/CFS Biomedical Research

Hosted and organised by
ME Research UK and the Irish ME Trust

Edinburgh Conference Centre,
Heriot Watt University, Edinburgh
Friday 25th May 2007



Dr Ellie Stein (Psychiatrist - Canada)

**Identified many flaws in the 7 RCTs
relied on by NICE**

Wrong criteria (2) Oxford not Fukuda

2 negative results

No benefits

**Measured only subjective responses-
NO objective measurements.**

**Totally disowned the Wessely-NICE
approach, “*I would never in my
practice use the Wessely model of
cognitive therapy – I find it
disrespectful to try to convince
somebody they don’t have an illness
that they clearly have”.***

**On the PACE trial “*It’s quite hard to
watch millions of pounds being spent
on a study that will tell us nothing”.***

IMPOSSIBLE TO SEPARATE THE POLITICS FROM THE MEDICINE AND SCIENCE

MAJOR POLITICAL EVENTS

GIBSON REPORT

NICE GUIDELINE

**THE MENTAL HEALTH MOVEMENT:
PERSECUTION OF PATIENTS?**

**A CONSIDERATION OF THE ROLE OF PROFESSOR SIMON WESSELY AND
OTHER MEMBERS OF THE "WESSELY SCHOOL" IN THE PERCEPTION OF
MYALGIC ENCEPHALOMYELITIS (ME) IN THE UK**

Background Briefing for the House of Commons Select Health Committee

MENTAL HEALTH MOVEMENT : PERSECUTION OF PATIENTS

**Briefing paper for Countess of Mar, Dec 2003 House of Lords Debate 22-1-04
House of Commons Select Committee on Health**

PRICE £4-00 TODAY

...and on the management and treatment of patients is increasingly determined not by
medical need but by economic considerations.

Document prepared for the Countess of Mar by Malcolm Hooper, Emeritus Professor of
Medicinal Chemistry, in collaboration with members of the ME community, Department
of Life Sciences, University of Sunderland, SR2 7EE, UK

December 2003

http://www.satori-5.co.uk/word_articles/me_prof_hooper_3.html -DOCUMENT

<http://listserv.nodak.edu/scripts/wa.exe?A2=ind0401d&l=co-cure&F=&S=&P=1313> -
DEBATE.

IN THE DEBATE IT WAS CLAIMED THAT IT WAS ACCEPTABLE FOR ME-CFS TO BE PLACED IN TWO DIFFERENT CLASSIFICATIONS IN ICD-10 NEUROLOGY , G.93.3 AND MENTAL AND BEHAVIOURAL, F.48.0

THE W.H.O. STATED CATEGORICALLY THAT THIS WAS NOT POSSIBLE OR ACCEPTABLE

ACCORDINGLY- LORD NORMAN WARNER, PARLIAMENTARY UNDER SECRETARY OF STATE FOR HEALTH, WROTE TO THE COUNTESS OF MAR ON 11 FEBRUARY 2004

“THE UK ACCEPTS ICD-10, AND THEREFORE AFTER IT WAS POINTED OUT THAT THE RELATIVELY NEW TERM CHRONIC FATIGUE SYNDROME (14 yrs on!) HAS BEEN INDEXED TO THE NEUROLOGY CHAPTER, CORRESPONDING ADJUSTMENTS WERE MADE TO THE WEB VERSION OF THE FIRST EDITION OF THE GUIDELINES, AND AN ERRATUM NOTE HAS BEEN PLACED ON THE RSM WEBSITE.”

**“THE SECOND EDITION OF THE WHO GUIDE TO MENTAL HEALTH AND NEUROLOGY IN PRIMARY CARE WILL HAVE ONLY ONE ICD-10 CODE FOR CFS- THIS IS G93.3
NOT YET DONE?”**

The National institute for Clinical Excellence- NICE

Established 1999 –funded by DoH (independent ?)

February 2004 requested to prepare Clinical and Service Guidelines for CFS/ME

September 2006 Draft Guideline published for Consultation

August 22nd 2007 final Guideline published

Comments and Criticism of proposals by many groups and individuals drawing attention to the many flaws in the proposals and offering alternative proposals from a consideration of the biological basis of the illness

“The draft guideline is fundamentally flawed because it presupposes certain interventions (CBT/GET) to be highly effective in CFS/ME for routine clinical use despite lack of adequate evidence.....it almost seems that a select group of psychiatrists with a polarised view of this complex condition is directing the development of the guideline from ‘behind the scene’.listen to patients.”

“.....tactically promoting Oxford criteria over the more widely used CDC criteria.....clear evidence of psychiatrist’ influence on this group.”

Member and Association of British Neurologist,

Despite some changes in tone Many Concerns About The Published Guideline Remain

BIOMEDICAL HAS BEEN TOTALLY IGNORED – SOME 4000 PUBLISHED PEER-REVIEWED PAPERS

The biomedical evidence did not come within the remit of the Guideline Development Group – diagnosis, management of adjustment and coping, symptom management ...rehabilitative strategiesoptimising function and achieving greater independence for adults and children

Reference is still made to “unhelpful beliefs”, “the relationship between thoughts, feelings, behaviours and symptoms and the distinction between causal and perpetuating factors”

CBT/GET is still recommended as a proven and effective treatment despite attention being drawn to the seriously flawed data on which these are recommended.

**Professor David Richards. British Association for Behavioural and Cognitive
Psychotherapies Magazine March 2007.**

Professor of Mental Health, University of York , UK BABCP member



**‘In power,’ CBT, just like New Labour, is
perceived as remote and imperious
.....lack of humility and openness.....**

**...the UCL trial of CBT in primary care....found no difference between
CBT and counsellingwhat use is a treatment if it cannot be
replicated reliably?**

**“Most CBT trials are poorly executed; quality thresholds for RCTs in NICE
guidelines are notoriously low, allowing the results of meta-analyses of
small poor quality studies to direct policy”**

“....there are now over 4,000 published studies that show underlying biomedical abnormalities in patients with this ill [ME-CFS]. It is not an illness that people can simply imagine that they have and its not a psychological illness. In my view, that debate, which has waged for 20 years, should now be over.”

Anton Komaroff – Harvard medical School – CDC Press Conference 2006

www.cdc.gov/od/oc/media/transcripts/t061103.htm

WITH ALL THIS INFORMATION I TRUST THAT THIS DEBATE WILL SOON BE OVER IN SWEDEN AS IT IS IN NORWAY.

THANK YOU

THE END



Energising Biomedical Research in ME/CFS

A lecture by Dr Vance Spence
Chairman of MERGE
Hon. Senior Fellow, University of Dundee

Part 1: Issues and Challenges
Part 2: MERGE research projects

In this lecture Dr Vance Spence examines some of the issues and challenges involved in ME/CFS research, and describes some of MERGE's recent and ongoing research projects.

A PERTH CAMCORDER CLUB PRODUCTION
JANUARY 2006

MERGE is a national UK charity funding biomedical research into Myalgic Encephalomyelitis (also known as ME/CFS). Its principal aim is to commission and fund high-quality scientific (biomedical) investigation into the causes, consequences and treatment of ME, but it also has a mission to "Energise ME Research".

MERGE, The Gateway
North Methven Street
Perth PH1 5PP, UK
Telephone/Fax: 01738 451234
E-mail: merge@pkavs.org.uk
Web: www.mereseearch.org.uk
Charity number: SC036942

"A highly successful fundraiser for cancer research told me that in the 1960s, when she began, the word 'cancer' could barely be whispered. But over years, thanks to the efforts of people like her, there was a sea change in awareness... We have to do the same — it is ground-level, back-breaking work, but only with data, data, data will we be able to answer our critics AND solve the enigma of ME/CFS."

Dr Vance Spence



Future/ Continuing Studies

Endothelial inflammation and blood distribution & Orthostatic Intolerance. Children

Oxidative Stress muscle and exercise. Nerve–muscle effects

Inflammatory cells – Oxidative stress & apoptosis/necrosis.

Mitochondrial function

Genetic Studies – what is changed/changing in ME patients

HIGH QUALITY RESEARCH IN MEDICINE AND BIOLOGY IS NOT BEING FUNDED – IT MUSTS BE NOW. HERE IS THE EVIDENCE!

www.mereseearch.org.uk

Ongoing projects

[The assessment of peripheral microvascular endothelial function in ME/CFS](#)

Dr David Newton, The Institute of Cardiovascular Research, University of Dundee, Dundee

[Unravelling the aetiology of post-exertional malaise in ME/CFS: the role of intracellular immunity and sensory processing](#)

Dr Jo Nijs, Department of Human Physiology, Vrije Universiteit Brussel, Brussels, Belgium

[Inflammation and arterial stiffness in patients with ME/CFS](#)

Dr Faisal Khan, The Institute of Cardiovascular Research, University of Dundee, Dundee

[Non-invasive structural and functional neuroimaging in ME/CFS](#)

Dr Kishore Bhakoo and Prof. Basant Puri, MRC Clinical Sciences Centre, Imperial College London, London

[Longitudinal cohort study to determine the prevalence of autonomic dysfunction and relationship with outcome in patients with myalgic encephalitis \(ME\)/chronic fatigue syndrome \(CFS\)](#)

Dr Julia Newton, School of Clinical Medical Sciences, University of Newcastle, Newcastle

[Physiological cost of walking at self selected and matched speeds in those with ME/CFS: a pilot study](#)

Dr Lorna Paul, School of Health and Social Care, Glasgow Caledonian University, Glasgow

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

Characterisation of differential gene expression in patients with chronic fatigue syndrome/myalgic encephalomyelitis

Dr John Gow, Department of Neurology, Southern General Hospital, University of Glasgow

Effects of muscle fatigue on H-reflex excitability in subjects with ME/CFS

Dr Les Wood, Department of Biological and Biomedical Sciences, Glasgow Caledonian University

An investigation into biochemical and blood flow aspects of ME/CFS in children

Dr Gwen Kennedy, The Institute of Cardiovascular Research, University of Dundee

Evaluation of pain and therapeutic intervention in people with ME/CFS

Dr Lorna Paul, School of Health and Social Care, Glasgow Caledonian University

Acetylcholine-mediated vasodilatation in ME/CFS patients: the role of nitric oxide, prostacyclin and endothelium-derived hyperpolarising factor

Dr Faisal Khan, The Institute of Cardiovascular Research, University of Dundee

As of March 2007, there are two projects going through our review process.

