

**Over-view of the Alison Hunter Memorial Foundation ME/ICD-CFS Clinical and Scientific Meeting, December 2001, Sydney, Australia**

*With grateful acknowledgment to Dr Rosamund Vallings and to Jan van Roijen*

The mission of the Alison Hunter Memorial Foundation is to reduce the impact in the community of the disease myalgic encephalomyelitis / chronic fatigue syndrome. The Foundation was established in 1998 and works with international researchers and ME/CFS societies to advance scientific knowledge and medical care. The Foundation is an enduring memorial to Alison Hunter and to all those whose lives have been devastated by ME/CFS. Alison died aged 19 in 1996 from severe ME, suffering seizures, paralysis, gastrointestinal paresis, severe recurrent mouth ulcers and overwhelming infection, having courageously fought ME/CFS for ten years.

**(For the avoidance of doubt, the term “ME/ICD-CFS” has been deliberately used throughout this text in order to differentiate the condition discussed at the Conference (classified since 1969 in the WHO International Classification of Diseases as a neurological disorder) from on-going “chronic fatigue” syndrome, also called by the same term (“CFS”) by psychiatrists of the “Wessely School” and defined by the UK psychiatric 1991 “Oxford” criteria (which in contrast to the international model expressly includes those with psychiatric fatigue). Repeated resistance and failure by these highly influential UK psychiatrists to acknowledge the differences between ME/ICD-CFS and psychiatric “CFS” has been publicly stated by eminent international researchers to have hindered scientific progress and medical understanding of ME/ICD-CFS for the last 15 years.**

The December 2001 Sydney Conference hosted world-renowned experts on ME/ICD-CFS such as Professor Anthony Komaroff from Harvard, Professor Kenny de Meirleir from Brussels, Professor Neil McGregor from the Department of Biological Sciences, University of Newcastle, New South Wales, Dr D Ablashi from Colorado and Dr S Levine from New York, who variously presented evidence on the biology of ME/ICD-CFS, gastro-intestinal symptoms and gastric emptying studies, ME/ICD-CFS and multiple sclerosis (MS) as subsets of a group of cellular immunity disorders, active HHV6 infection and its correlation with RNaseL low molecular weight protein (37KDa) in ME/ICD-CFS patients, objective evidence of brain impairment, regional cerebral blood flow, pathophysiological mechanisms of ME/ICD-CFS, biochemical anomalies, food intolerance and channelopathy in ME/ICD-CFS.

**Komaroff A. (Professor of Medicine, Harvard)**  
**“The Biology of ME/ICD-CFS”**

Komaroff gave a presentation which reviewed the epidemiological context and symptoms, pointing out that some patients are completely disabled by the symptoms and noting that impairment of these patients, as measured by the SF-36 instrument, is comparable with that of patients with congestive heart failure.

Past medical history is notable primarily for a high frequency of atopic or allergic illness in up to 80% of patients.

Physical examination is notable for posterior cervical adenopathy in about 35% and for abnormal tests of balance (Romberg and tandem gait) in about 25%.

No single laboratory test has yet been identified which has high specificity for ME/ICD-CFS, but a growing literature reports a number of objective laboratory findings which clearly distinguish patients from healthy controls. In his experience, several findings are seen more often in patients: low levels of circulating immune complexes, elevated total complement (CH50), elevated IgG, atypical lymphocytosis and low levels of antinuclear antibodies (ANA).

Neuroendocrine findings demonstrate that patients have a variety of abnormalities of the HPA axes, for example there is reduced hypothalamic production of corticotrophin releasing hormone (CRH) leading to diminished pituitary release of ACTH, leading to basal hypocortisolism; this axis is the opposite of that seen in depression. CT scans have demonstrated that the adrenal glands of patients are half the size of those in healthy controls.

Neuroimaging studies report that in 78% of cases MRI scans reveal punctate areas of high signal in the white matter, particularly in the subcortical areas: these findings are not very sensitive and are not specific for ME/ICD-CFS but are useful in differentiating the condition from MS, since in Komaroff's experience about 10% of ME/ICD-CFS patients have had a transient focal neurologic deficit. Single photon emission computerised tomography (SPECT) reveals defects of perfusion and metabolism much more often in patients with ME/ICD-CFS than in healthy controls.

Autonomic nervous system testing studies from Johns Hopkins, Harvard and other institutions find evidence of both sympathetic and parasympathetic neuropathy in ME/ICD-CFS patients. Clinically, 50% of patients meet criteria for neurally mediated hypotension and postural tachycardia syndromes.

There is evidence from several controlled studies of the reactivation of various chronic viral infections; in Komaroff's opinion this evidence is strongest for HHV6 (a neurotropic and immunotropic virus). HHV6 can lead to neural sequelae, and there is good evidence of a strong association between HHV6 and MS.

Immunological studies have revealed a variety of immunological abnormalities, especially impaired function of natural killer cells and increased numbers of activated CD+T cells. Whilst neither finding is specific enough to constitute a diagnostic marker, they are nevertheless consistent with a chronically activated immune system in ME/ICD-CFS.

Two groups have reported what appears to be a more specific immune system abnormality in ME/ICD-CFS: an increased activity of the 2-5A enzymatic pathway in lymphocytes. Patients with ME/ICD-CFS were very different from those with depression, fibromyalgia and healthy controls.

From a psychiatric perspective, probably only a small proportion of patients who seek help for fatigue have ME/ICD-CFS. Most ME/ICD-CFS patients become depressed and anxious *after* the onset of the illness, with up to 50% developing depression or anxiety in the years after the onset

of ME/ICD-CFS. According to several careful studies, most patients with ME/ICD-CFS have no prior history of significant psychiatric disease prior to the onset of ME/ICD-CFS.

What is ME/ICD-CFS? In Komaroff's view, the evidence indicates an organic basis. In many but not all patients there are abnormalities of the limbic system of the brain, and abnormal regulation of the immune system. Multiple differing triggering agents, including toxins and stress, could be involved in different cases.

**De Becker P (1), Nijs J (1), McGregor N (2), De Meirleir K (1)**

**(1) Department of Human Physiology Vrije Universiteit, Brussel, Belgium**

**(2) Department of Biological Sciences, University of Newcastle, New South Wales)**

**“Usefulness of the Fukuda and Holmes definitions in the Diagnosis of ME/ICD-CFS”**

The US Holmes et al (1988) and Fukuda et al (1994) criteria ( Fukuda *et al* including UK psychiatrists Michael Sharpe and Simon Wessely) are widely used all over the world, yet a specific European study regarding ME-ICD-CFS patient symptomatology had not been conducted, so the authors looked at 2073 consecutive patients. Discriminant function analysis revealed that the two definitions can be differentiated by symptom severity and prevalence. The Holmes definition was more strongly associated than the Fukuda definition with symptoms that differentiated ME/ICD-CFS patients from patients who did not comply with the definitions.

The ME/ICD-CFS patients fulfilling the Holmes criteria have an increased prevalence and severity of many of the symptoms which determine the difference between ME/ICD-CFS and “chronic fatigue” patients.

Patients fulfilling the 1994 Fukuda criteria were less severely affected, leading to an increase in clinical heterogeneity.

The inclusion of specific additional symptoms to the Holmes criteria was found to improve the sensitivity / specificity and accuracy for selection of ME/ICD-CFS patients, those additional symptoms being hot flushes, paralysis, new sensitivities to food / drugs, urinary frequency, cold extremities, photophobia, light headedness, muscle fasciculations, exertional dyspnoea, gastrointestinal disturbance, attention deficit and difficulties with words. The inclusion of these symptoms would strengthen the ability to select ME/ICD-CFS patients, and the inclusion of a severity index would be beneficial for subcategorisation of patients.

**Burnett RB (Endocrine and Metabolic Unit, Royal Adelaide Hospital, Adelaide)**

**Chatterton B (Dept Nuclear Medicine, Royal Adelaide Hospital, Australia)**

**“Gastro-Intestinal Symptoms and Gastric Emptying Studies in ME/ICD-CFS”**

Gastro-intestinal symptoms are particularly common in ME/ICD-CFS patients but have never been properly assessed even though after the fatigue and central symptoms they are the commonest group and cause considerable distress.

These patients all had increased large bowel symptoms of faecal urgency, nocturnal diarrhoea, loose consistency of the stools and increased frequency.

88% of patients had one or more upper gastro-intestinal symptoms and 91% of patients had an abnormal gastric emptying study; 46% had a delay in oesophageal emptying; 89% had a delay in the liquid phase and 67% had a delay in the solid phase.

This study indicates that the cause is an abnormality of gut motility. The main abnormality was a delay in the liquid phase rather than the solid phase. This suggests a central rather than a peripheral causation for the gastric delay. The delay in mobility may well lead to bacterial overgrowth.

**Butt, HL, Dunstan RH, McGregor N, Roberts TK (Department of Biological and Chemical Sciences, University of Newcastle, Newcastle, Australia)**

**“Bacterial Colonisation in Patients with Persistent Fatigue”**

Bacterial Colonisation (BC) in patients with persistent fatigue is a disease entity that has not been described in the medical literature. This condition of unknown aetiology is manifested in patients with ME/ICD-CFS, fibromyalgia, irritable bowel syndrome and autism.

Muscular pain (face, neck, shoulder and lower back) in fatigued patients with BC was significantly more severe than in patients with no BC.

The distribution of faecal intestinal microbial flora in this study population was markedly altered. A high faecal enterococcal count significantly and positively correlates with neurological and cognitive functions.

Similarly a high aerobe/anaerobe ratio significantly and positively correlates with poor colonic function, poor digestion and malabsorption of the gastro-intestinal tract.

**Behan WHM (Professor of Pathology, Glasgow)**

**“Research Update on ME/ICD-CFS”**

Much controversy has been caused by the fact that fatigue has both central and peripheral components and the mechanisms are complex; however, in other disorders such as multiple sclerosis (MS) there is a significant decrease in muscle phosphocreatine resynthesis after exercise, while in chronic obstructive pulmonary disease (COPD) reductions in muscle aerobic capacity appear to play almost as important a role as defects in lung ventilation. Behan used detailed exercise studies to compare and contrast the response in well-characterised groups of patients with ME/ICD-CFS, MS and COPD. The muscle chemistry features associated with fatigue all seem to be the same.

There is a general manifestation of problems with the muscles, such as changes in enzymes and muscle mass. Professor Behan described a pathway for exercise from brain to nerves to muscle to muscle metabolism, and from lungs to circulation to muscle metabolism; she had found that in ME/ICD-CFS there seemed to be abnormalities in all these processes.

She described two kinds of muscle fibre – “fast” (used for bursts of energy) and “slow” (used for endurance). ME/ICD-CFS patients had up to 20% less of the “slow” muscle fibres, which helps to explain why sufferers tire so easily.

Deconditioning is not a perpetuating factor in ME/ICD-CFS.

The muscle involvement includes weakness, delayed recovery, decreased aerobic activity, mitochondrial abnormalities and metabolic abnormalities.

Tests showed that patients are doing their best, and that 24 hours after exercise all patients were worse in strength, with the reduction being most severe after 24 hours. This is because the metabolites are slow at resynthesising. Patients have the metabolites but cannot use them properly, so supplements are unlikely to be of help either.

Resting energy expenditure (REE) is elevated in ME/ICD-CFS patients unable to exercise and this may relate to cytokine abnormalities and to autonomic dysfunction.

In relation to cardiovascular involvement, the heart is slow to get going with exercise and remains at low peak value. This may be due to increased vagal tone or an intrinsic heart muscle effect. Autonomic function may play a role.

CNS involvement has been shown in SPECT and MRI scans, and neuroendocrine studies show HPA axis abnormalities.

Stress can affect the CNS providing a changed micro-environment in the brain and increased permeability of the blood brain barrier. This can lead to changes in gene expression, which in turn affects production of neurotransmitters. All these events have an impact on the exercise pathway.

One new finding in ME/ICD-CFS is that convincing evidence of cardiovascular impairment can be demonstrated.

The whole process is likely to have been precipitated by a severe insult to the body.

It is hoped that these studies will lead to a better understanding of the interference in normal exercise capacity.

**Sargent C, Scroop GC, Burnett RB, Buckley JD and Nemeth PD**  
**(Adelaide Chronic Fatigue Syndrome Research Unit, Department of Physiology, University of Adelaide, South Australia)**

**“Excess lactic acid is not a cause of fatigue in Chronic Fatigue Syndrome”**

It is commonly assumed that the restricted lifestyle of CFS patients leads to a progressive reduction in physical fitness, thus perpetuating the condition. It is on that basis that both the Australian and British Colleges of Physicians recommended exercise training programmes.

The conclusion from this study is that ME/ICD-CFS patients have normal physical fitness and that there is no physiological basis for recommending graded exercise training programmes.

Some other explanation must therefore be sought for the excessive fatigue, both during and after exercise, which is such a classical feature of the disorder.

Early work suggested that excessive lactic acid accumulation might be a factor in the muscle pain and fatigue experienced by patients during exercise so the authors completed an investigation of plasma lactate responses during incremental exercise to volitional exhaustion in patients and matched sedentary controls.

Increases in plasma lactate concentration with exercise intensity were not different from control subjects and these results indicate that the production and clearance of lactic acid in ME/ICD-CFS patients is normal and does not contribute to their fatigue and reduced power output during exercise.

**Nicolson GL et al (The Institute for Molecular Medicine, Huntington Beach, California)**  
**“Diagnosis and treatment of multiple, chronic bacterial and viral infections in chronic fatigue Syndrome (ME/CFS), Fibromyalgia Syndrome and Gulf War Illnesses”**

Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia Syndrome and Gulf War Illness have overlapping signs and symptoms. Using techniques of gene tracking, the authors found a major source of morbidity to be caused by various chronic viral and bacterial infections, especially mycoplasma variants, with mycoplasmal infections inside blood leucocytes but not in blood plasma or serum.

They conclude that subsets of GWI, ME/CFS, FMS and also patients with rheumatoid arthritis have transmittable chronic bacterial and viral infections and that the illnesses may be due in part to multiple chemical / biological exposures that cause multi-factorial illnesses.

**Englebienne P, de Meirleir K et al (Free University of Brussels, Belgium)**  
**“Chronic Fatigue Syndrome (CFS) and Multiple Sclerosis (MS) as Subsets of a Group of Cellular Immunity Disorders”**

Apoptosis (programmed cell death) is a critical component of adaptive cellular immunity. When challenged by infection, type I interferons elicit apoptotic responses by inducing the expression of 2-5A synthetase (2-5OAS), RNaseL and the p68 dependent kinase (PKR).

Results from the authors' laboratories point to an improper activation of 2-5OAS in monocytes of both patients with ME/ICD-CFS and with chronic (but not in relapsing / remitting) MS, which results in an inappropriate activation of RNaseL.

This process ultimately leads to a blockade of the RNaseL-mediated apoptotic programme and it supports the involvement of environmental factors. Such cellular stress is capable of generating small RNA fragments and / or of inducing the transcription of endogenous retrovirus sequences. The ‘abnormal’ RNA sequences are responsible for the inappropriate activation of 2-5OAS and have been implicated in the aetiology of both ME/ICD-CFS and MS.

Depending on their origin and structure, these RNA fragments are capable of either activating or down-regulating PKR. This results in a differential effect not only on the PKR/RNaseL-mediated apoptotic programmes but also on the activation of by PKR of the inducible NO synthetase. A release of nitric oxide at either high rates (as in ME/ICD-CFS) or low rates (as in chronic MS) by lymphocytes has corollary consequences, triggering the skeletal and cardiac

muscle ryanodine receptors (calcium channels), NK cell function, COX2 activation and glutamate release by activated T-cells in the brain.

Glutamate upregulation leads to oligodendrocyte excitotoxicity in MS, whilst glutamate downregulation in ME/ICD-CFS impairs hypothalamic CRH secretion.

These results suggest that ME/ICD-CFS and MS are extremes of an array of dysfunctions in the 2-5A/RNaseL/PKR pathways into which other autoimmune diseases such as lupus might fit.

**Ablashi D (1), Gupta S (2), Peterson D (3), Levine S (4) et al**

**(1) ABI Inc, Columbia, MD,USA (2) University of California, Irvine CA**

**(3) Sierra Internal Med, Incline Village, NV, USA (4) CFS Clinic, New York)**

**“Evidence of Active HHV-6 Infection and its Correlation with RNaseL Low Molecular Weight Protein (37KDa) in ME/ICD-CFS”**

The authors studied HHV-6 frequency of active infection in ME/ICD-CFS patients by coculture of PBMCs, IgM response, presence of HHV-6 DNA by nested and real time TaqMan PCR.

Since the levels of RNaseL and LMW protein (ie. 37KDa) is consistently detected in PBMC/s of patients with ME/ICD-CFS, the authors correlated the 37 KDa protein with active HHV-6 infection.

More than 65% of ME/ICD-CFS patients had active HHV-6 infection, with cerebro-spinal fluid from 26.7% showing HHV-6 DNA.

HHV-6 DNA was also detected in the plasma of 34% by nested PCR, but using TaqMan PCR, it was demonstrated that more than 48.5% plasma and 40% cerebro-spinal fluid contained HHV-6 DNA (showing higher sensitivity of the TaqMan assay).

HHV-6 IgM levels ranged from 1:20 to 1:320.

HHV-6 Variant A infection was identified by TaqMan PCR in almost all the positive patients. HHV-6 infection was present in 65% of ME/ICD-CFS patients.

Correlation of HHV-6 infection and 37 KDa protein was significant.

In conclusion, higher frequency of HHV-6 reactivation was detected in ME/ICD-CFS patients, using various assays. HHV-6 Variant A infection was predominant in ME/ICD-CFS. HHV-6 infection also correlated with 37KDa protein.

**De Meirleir K(1), De Becker P(1), Nicolson GL(2) et al**

**(1) Department of Human Physiology, Vrije Universiteit Brussel, Belgium**

**(2) Institute for Molecular Medicine, Huntington Beach, California)**

“Association between Mycoplasmae and 2-5A synthetase RNaseL antiviral pathway in ME/ICD-CFS”

Numerous reports have highlighted the importance of Mycoplasmae and the dysregulation of the 2-5A synthetase RNaseL antiviral pathway in subsets of the Chronic Fatigue Syndrome. The authors conducted a study in Brussels to see if there was a physiopathological mechanism between infection by Mycoplasma species and the deregulation of the 2-5A synthetase / RNaseL antiviral pathway in ME/ICD-CFS.

Mycoplasmae-infected ME/ICD-CFS patients presented with a significantly elevated RNaseL-ratio compared with non-infected controls.

These results suggest a strong interaction between Mycoplasmae infections and a deregulation of the 2-5A synthetase RNaseL antiviral pathway. It has been suggested that LMW RNaseL may reduce Th1 activity, with susceptibility to infections and a suppressed ability to eliminate intracellular antigens.

Mycoplasmae are active in stimulating the immune system and can act as polyclonal T-cell and B-cell activators. To bring about their phagocytic activity, monocytes produce elastase, which enables them to pass through connective tissue. Elastase is capable of cleaving 80KDa RNaseL, thus causing deregulation of the antiviral pathway.

**Abou-Donia MB (Department of Pharmacology and Cancer Biology, Duke University Medical Centre, North Carolina, USA)**

“Stress and Combined Exposure to Low Daily Doses of Pyridostigmine Bromide, DEET and Permethrin in Adult Rats Causes Blood Brain Barrier Disruption and Neurochemical and Neuropathological Alterations in the Brain”

A combined exposure to high doses of PB, DEET and permethrin leads to a significant toxicity and neurological dysfunction. The present study looked at the effects following exposure to low doses of these chemicals when combined with stress (simulating the daily exposure experienced by Gulf War veterans).

Animals subjected to either chemical treatment or stress alone did not show changes in body weight, brain hexamethonium iodide uptake, brain AChE or plasma ChE but did exhibit a slight increase in blood brain barrier (BBB) permeability in comparison with control animals, and exhibited either no or minimal neuronal cell death.

In contrast, animals subjected to both chemical treatment and stress exhibited a dramatic increase in BBB permeability, with focal perivascular accumulation of HRP in both cerebrum and the brainstem, a significant decrease in brain AChE activity, a decrease in m2 muscarinic Ach receptor ligand binding density in midbrain and cerebellum, and a significant neuronal death associated with a reduced MAP-2 expression in the cerebral cortex and the hippocampus.

These results underscore that when combined with stress, exposure to even low doses of chemicals (which by themselves produce minimal effects) leads to a significant brain injury. Leakage through the BBB makes the organism vulnerable to entry by toxins.



Histological changes were also present in the liver and were particularly severe when the combination was used.

**Kilburn KH (Professor of Medicine, Director of Environmental Sciences Laboratory, University of South California, USA)**

**“Objective Evidence of Brain Impairment in the Chemical Syndrome”**

Three arguments were presented:

- first: the multiple labels applied to human responses to chemical exposure describe but one syndrome; “splitting” confuses the issue
- second: the response to chemicals is mediated by the brain, which is the main target of the offending chemicals
- third: when compared with predicted values, measurements of key brain functions provide objective demonstration of effects of chemicals.

ME/ICD-CFS is an increasingly frequent illness and vies with multiple chemical sensitivity (MCS) as the most popular title for the status of being adversely affected by environmental exposure to chemicals.

Excluding epiphenomena, responses are in categories and are physiological brain functions (like balance) in a list of more than 35.

Experience shows that there are 8 physiological tests and 11 psychological tests that yield reliable results; these have been applied to more than 20 groups of people exposed to chemicals.

Illustrative examples of implicated chemicals are formaldehyde and organophosphates.

**Casse R, Burnett R et al (The Queen Elizabeth Hospital, Adelaide, Australia)**

**“Regional cerebral blood flow in chronic fatigue syndrome”**

ME/ICD-CFS is a complex disorder characterised by profound fatigue and neuropsychiatric dysfunction, including mental fatigue, impaired concentration and slowness of thinking. Patients with this disorder have been studied with radionuclide perfusion scans but most previous studies were performed on inhomogeneous patient populations and were not analysed with Statistical Parametric Mapping (SMP). To address these issues, a study was performed with Tc-99m HMPAO SPECT and a triple head gamma-camera.

Visually, a deficit in regional cerebral blood flow (rCBF) in the medial temporal lobe was definite in over 50% of patients. The location, amplitude and corrected p-value of significant focal deficits in ME/ICD-CFS were: brainstem 19%; right medial temporal lobe 22%; frontal lobe 17% and anterior cingulate gyrus 12%.

There appears to be objective evidence that patients with moderately severe ME/ICD-CFS have focal cortical and brainstem hypoperfusion.

**Cosford RE (Director, Northern Beaches Care Centre in conjunction with the Collaborating Pain Research Unit, University of Newcastle, Australia)**

**“Neuroimmune Gastrointestinal Dysfunction Syndrome: a New Name for Autism and Chronic Fatigue Syndrome? A Spectrum of Disease**

ME/ICD-CFS is characterised by fatigue, gastrointestinal symptoms with irritable bowel, food intolerance, muscle pain and weakness, recurrent illness and neurocognitive symptoms including sensitivity to bright lights, noise and odours, and disordered and fragmented sleep. Autism is similarly characterised by neurocognitive symptoms with sleep disorder, marked sensory sensitivity and gastrointestinal symptoms, with demonstrable reactions to certain foods, particularly gluten-containing and casein-containing foods. In both disorders, epidemiological studies have indicated the probability of a genetic susceptibility, but with prominent environmental triggers.

In ME/ICD-CFS, various metabolic abnormalities have been identified. Increased gastric emptying times and increased gastrointestinal permeability have been documented as markers of gastrointestinal dysbiosis, whilst faecal studies demonstrate gastrointestinal dysbiosis with overgrowth of streptococcal/enterococcal species in some 60% of patients.

Urinary organic acid analyses demonstrate increased markers of fibrillar and non-fibrillar catabolism in ME/ICD-CFS patients. Patients with prominent visual and sensory disturbances also show a characteristic pattern of urinary organic acid disturbance. Plasma lipid analysis reveals predominantly low elaidic acid, which has been shown as a marker for pain.

Urinary organic acids indicate a strongly catabolic picture, with fibrillar and non-fibrillar catabolism, generally low urinary glycosamines, and abnormalities in the markers for the tricarboxylic acid cycle similar to those seen in ME/ICD-CFS.

In addition to these changes, raised urinary hydroxyproline (a marker of increased connective tissue breakdown) and raised ornithine (a marker for abnormalities in the urea cycle and ammonia metabolism) are typically seen.

Plasma lipid analysis reveals lowered levels of elaidic acid but more significantly, also a block in the beta-oxidation of long chain fatty acids, with accumulation of long chain fats, deficiency in cholesterol and markedly reduced eicosapentaenoic and docosahexanoic acids.

Notably, raised levels of nervonic acid are consistently found. Nervonic acid is the fatty acid major component of sphingomyelin and may indicate a disruption of myelination.

Endoscopic studies have revealed gastric inflammation, duodenal inflammation and colonic inflammation in a significant percentage of children with autism. Immune abnormalities are well documented in autism by various researchers.

Similarities with the subgroup of ME/ICD-CFS patients with gastrointestinal symptoms and neurocognitive problems suggest a possible commonality in aetiology.

It has already been hypothesised that ME/ICD-CFS is a toxin-mediated channelopathy (Chaudhuri) and it is therefore hypothesised that in a subgroup of ME/ICD-CFS patients and in most children with autism, the illness is largely toxin-mediated.

**Robinson GL, McGregor NR et al (University of Newcastle, New South Wales)**

**“Biochemical anomalies in people with chronic fatigue syndrome who have visual problems: implications for immune system dysfunction and dietary intervention”**

There has been identification of biochemical anomalies in people with ME/ICD-CFS and the range of symptoms includes visual problems which are similar to those reported by people identified as having a visual sub-type of dyslexia called Irlen Syndrome (IS).

These visual problems have been associated with abnormal fatty acid metabolism.

The primary investigation identified a number of biochemical markers associated with symptom incidence related to a dysregulation of fatty acid metabolism.

A more detailed analysis found significant differences in the metabolic profiles, indicative of differences in connective tissue turnover due to infection or stress. There were also indications of alterations of neuronal functioning due to changes in neurotransmitters.

Preliminary results for the third study found differences in linoleic acid, tyrosine, aspartic acid and glutamic acid. The IS subjects also had a significantly higher incidence of allergies, gastrointestinal problems, kidney infections, photophobia, headaches, fatigue and impaired concentration.

The results of these studies confirm the association between ME/ICD-CFS and visual processing problems, with essential fatty acid metabolism likely to be an indicator. A large percentage have visual processing problems. The results also suggest a need for investigation of immune system dysfunction.

**Butt HL, McGregor NR, Dunstan RH (School of Biological and Chemical Sciences, University of Newcastle, New South Wales)**

**“Food intolerance exists as a co-morbidity in Chronic Fatigue Syndrome”**

It has been estimated that food intolerance is a significant factor in 20-30% of patients with ME/ICD-CFS.

Patients reporting gastro-intestinal or food-induced problems were assessed for possible food and chemical intolerance via an elimination diet protocol.

89.5% reported a positive outcome from dietary exclusion: gastrointestinal symptoms synonymous with irritable bowel syndrome (IBS) decreased following the intervention.

Food and chemical intolerance may therefore be of aetiological significance in the development of IBS symptoms in ME/ICD-CFS, but such investigation of intolerances remains an under-utilised intervention.

**POSTER PRESENTATIONS**

Ten posters were presented, with some covering in more detail the research presented orally.

1. Wilhelmina Behan / Department of Pathology and Centre for Exercise Science and Medicine, University of Glasgow. “Cardiovascular function and exercise intolerance in chronic fatigue syndrome”

Professor Behan presented evidence that there is cardiovascular impairment during dynamic exercise, as judged by the cardiac output response to moderate exercise.

2. Pascale de Becker / Department of Human Physiology, Vrije Universiteit, Brussel “Aetiology of CFS: the Belgian Experience”

A number of different stressors and consequent immunological and neuro-endocrinological changes can contribute to the onset of ME/ICD-CFS.

3. Pascale de Becker / *ibid* “Monitoring a Hypothetical Channelopathy in Chronic Fatigue Syndrome”

This team presented another poster providing further evidence for a channelopathy in a subset of patients. More than 50% of patients presented with abnormal whole body potassium content. Discriminant function analysis revealed that patients and control subjects could be discriminated on immunophenotyping, with the predominant cell differences being the increase in CD19+CD5+ (mature B-) cells and the decrease in CD3-CD16+CD56+ (NK) cells. The fall in NK cells was very strongly associated with increases in the RNaseL ratio and with falls in serum calcium levels.

These observations provide evidence for a channelopathy in an important subset of CFS patients, probably induced by the deregulated 2-5ARNaseL antiviral pathway.

4. Pascale de Becker / *ibid* “Prevalence of Mycoplasma Infections Among Belgian CFS Patients”

This organism was found in 68.7% of a group of 272 patients.

5. Tania Emms / CPRU, University of Newcastle “Supplementation with L-serine shows potential for symptoms management in CFS”

Previous studies investigating a molecular basis to ME/ICD-CFS reported that urinary excretion of the amino acid serine is an important discriminatory metabolite distinguishing subjects from controls. Serine deficiency is suggested as an important factor contributing to the severity of symptoms in ME/ICD-CFS. A double-blind placebo controlled trial was warranted after findings of significant reduction in symptom expression in 28 patients following 3 months using L-serine 1.3gm daily.

6. Ann Harvey / Wellington, New Zealand

A meta-analysis looking at cortisol levels in ME/ICD-CFS patients found that patients seen in tertiary care show more endocrine abnormalities.

**7. Lawrence A Klapow / Biosciences, Santa Rosa, California**

A suspected new roundworm species, *Cryptostrongylus pulmoni*, infects a large percentage of ME/ICD-CFS patients (estimated at 63% in the current study) but not controls. It is significantly associated with the syndrome.

**8. CH Little / Mt Waveney, Victoria, Australia**

This laboratory has identified a separate class of immune products (T cell antigen binding molecules) which may be the basis for adverse reactions experienced by some patients to foods. Research indicates that an appropriate immune response to ingested food proteins is an absence of both Th1 and Th2 immune responses. This outcome (ie. no response) may depend on antigen-specific regulatory cells whose function is to maintain tolerance to food proteins. The presence or absence of an immune response depends critically on signals delivered by special antigen-presenting cells (dendritic cells). This process can be potentially disrupted by environmental influences.

**9. P Clifton Bligh / Royal North Shore Hospital CFS Research Unit, New South Wales**

This presentation concluded that the fall in urinary succinic acid seen in ME/ICD-CFS patients was associated with deregulation of energy availability and protein synthesis suggestive of a cytokine - mediated nitric oxide mediated change in chemistry, causing an increase in protein turnover and increase in glucose dependence; a fall in oxydative phosphorylation is occurring, which relate to the expression of fatigue.

**10. W. Tarello / Perugia, Italy**

Tarello, a veterinary surgeon, presented evidence of CFS in a horse from the USA, examined in Dubai. It was treated with potassium arsenite and made a good recovery.

**In conclusion**

Richard Burnett's final words echoed the consensus of the conference that the brain, limbic system and gut are implicated in ME/ICD-CFS, with the syndrome being triggered by various factors.