I was privileged to attend the 8th IACFS conference in Fort Lauderdale, Florida from 10-14th January 2007. There was a larger number of presentations and attendees than at any previous CFS conference, and the quality of presentations and research achieved in the past 2 years was indeed exciting. The conference was ably organized and hosted by Dr Nancy Klimas, and thanks must go to her. This conference combined the research and clinical work which thus gave a good overview of all aspects of the illness. The days were long and intensive, but most people (even those with CFS) managed to stay the distance and there was so much to learn. The conference was truly international with participants and presenters from around the globe.

FATIGUE SESSION

The first session covered various aspects of fatigue. This was overviewed by Prof Y Watanabe from Osaka, Japan. He described about 1/3 of the population in Japan as suffering from fatigue; 42% due to overwork, 19% due to disease and the rest of unknown cause. There are 3 major bioalarm systems: pain, fever and fatigue, the latter being an important bioalarm to order rest. Fatigue is felt in the brain, and maybe acute, subacute or chronic. Various methods were described to study fatigue such as cortical function, behavioural, autonomic nerve function, biochemical markers in plasma and saliva and brain function with scans. The aim of such studies on fatigue is to develop likely therapeutic interventions and anti-fatigue programmes.

Not only drug and dietary measures are being studied, but such issues as environment, aromas, animal (pet) intervention, creativity etc. Motivation helps to overcome fatigue particularly with creativity.

S.Tajima (Osaka) presented a study using actigraphy showing that quality of sleep was decreased because of increased wake episodes during the sleep period. This leads to lack of para-sympathetic activation during the sleep period, and further deterioration of sleep quality in CFS.

Complexity surrounding the word “fatigue” can be reduced by creating new terms to describe fatigue and this was outlined by N.Porter (De Paul Univ, USA). Results using the ME/CFS types questionnaire (MFTQ) showed that there are 5 types of fatigue associated with CFS:
1.Wired (overstimulated, tense, agitated),
2. Brain fog,
3. Molasses fatigue (heaviness)
4. Flu fatigue (immunological)
5. Post-exertional.
This new classification of fatigue can help to study fatigue more thoroughly.

E.Maloney (Atlanta, Georgia) confirmed the association between CFS and high allostatic load. Allostasis is the maintenance of stability through change. Environment, trauma, stress, behavioural response, genes and developmental experiences all have an effect on the physiological changes leading to allostatic load. 56% of CFS patients were found to have high allostatic load (females>males). Incidentally it was also found that those with CFS in this study in Georgia had a greater prevalence of metabolic syndrome. The greater the allostatic load the greater the prevalence of metabolic syndrome, and females with metabolic syndrome were 4 times more likely to have CFS than females without metabolic syndrome.

Claims for disability in the USA in CFS have been limited by lack of a confirmatory test to establish a diagnosis. However an abnormal exercise stress test is an example of a laboratory test that can be used. M.Ciccolella (Stockton,CA) compared tests to show that results from serial exercise tests can be used to assess the effects of post-exertional malaise in CFS. It is concluded that a single exercise test is insufficient to demonstrate the extent of functional impairment in CFS patients. A second test 24 hours later showed that CFS patients had significantly worse performance and this distinguishes CFS from other illnesses.

U.Hannestad (Linkoping, Sweden) investigated the possibility of abnormalities in excretion of GABA and β-alanine in urine because of the sleep disturbance and fatigue in CFS, GABA being the major neurotransmitter in the CNS, and β-alanine exerting inhibitory effects in the CNS. Increased excretion of β-alanine was found in a small subgroup of the CFS patients studied. Urine may not be the best body fluid to estimate these chemicals however, and cerebrospinal fluid would be better if practical.

P.Nestadt (New York,USA) compared brain metabolite levels between CFS with generalized anxiety disorder and healthy controls and examined the association of derived neurochemicals and psychiatric symptomatology. Previous uncontrolled studies had showed elevated lactate in the brain in CFS. This study showing a significant proportion of CFS patients had elevated ventricular lactate, and marked differences in hippocampal glutamate helped to distinguish between CFS patients with and without depression. Those with CFS also had significantly lower N-acetyl-aspartate in the right hippocampus, indicating reduced neuron density or metabolism.

The role of alterations in apoptosis playing a role in post-infection fatigue states (PIFS) was addressed in a study using gene array techniques presented by T.Whistler (Atlanta,Georgia). The severity of an acute infection is related to the likelihood of recovery, and affects the fundamental cellular processes. These resultant altered gene expression profiles are manifest in several persistent symptoms in PIFS. This indicates that many symptoms maybe immunologically mediated. The genes work as a team and there are a number which overlap.

An overview of the Fatigue Session was summarized by Fred` Friedberg. He discussed how we can measure fatigue – using retrospective questionnaires may not relate to real time. Self report of physical function may not be “actual”. In real time measures, subjects may not remember fatigue accurately, so physician visits and behavioural assessments are important. Use of palm pilots can give more accurate real time measures, and practice gives better recall for fatigue.

In an actigraphic study over 2 years to assess functional improvement, the better a person’s health, the less they reported fatigue having an effect on function, however despite spending less time lying down, they were still not actually better. There was global improvement leading to improved self report functioning which was likely to be due to improved coping ability. It is probable subjects were conducting their activities differently over time. Graded activity was not shown to increase actual activity ability, and there was no confirmation of improved symptoms. Fatigue and pain tended to increase after 30% of increased activity. More sleep time may lead to activity substitution.

FATIGUE POSTERS

The use of Heart Rate Variability (HRV) software was described by E.Stein (Calgary, Canada) as a useful in office diagnostic tool. HRV has been reported to show significant differences between CFS patients and controls. This software can efficiently distinguish between patients and controls. The severely ill patients were found to be 2SD `below the mean.

S.Stevens (Salt Lake City,USA) found that for CFS patients post exertional malaise is an incapacitating feature of the syndrome. There is a delayed recovery response to exercise distinctly different from controls. Patients took on average 4 days to recover from the graded maximal cardiopulmonary test compared with one day for the controls. 50% required more than 5 days to recover.

K de Meirleir (Brussels, Belgium) found that fructose malabsorption is very common in their CFS patients. Lactase deficiency is less common, and equal to the level in the normal population. These conditions can lead to intestinal dysbiosis, and careful diet is therefore required.

R.Van Konynenburg (Livermore,USA) claims to have found compelling evidence for glutathione depletion –methylation cycle block as part of the pathogenesis of CFS, in a number of patients. He hypothesizes that the higher prevalence of CFS in women is due to genetic polymorphisms in certain enzymes involved in the metabolism of oestrogens.

In a pilot study, J.Teilelbaum has treated 41 CFS and FM patients with D-Ribose. This has markedly improved many symptoms such as energy and sleep patterns. A larger RCT is planned. An overview of MCS was presented by P.Gibson (Harrisonburg, USA). She emphasized that there is need for further research in this little understood condition, which has a serious impact on quality of life. She also noted that there is a great lack of understanding of this condition by health professionals, and education is essential. A.Cusco-Segarra (Barcelona,Spain) has found the abbreviated environmental exposure and sensitivity inventory useful to detect MCS. The validity needs some fine tuning.

A.Chester (Washington DC, USA) looked at the prevalence of patients with unexplained chronic fatigue and chronic rhinosinusitis. They are more likely to notice a sudden onset of fatigue. The presence of non-frontal headache was also more common than in fatigued patients without sinusitis.

Decreased renal function (40-50%) was a frequent finding in a group of 15 CFS patients studied by T.Park (Seoul,Korea). His hypothesis is that CFS is a microvascular disease impacting individual organs. He notes that diabetics with renal vascular disease also complain of profound fatigue.

Increased incidence of thyroid malignancy associated with CFS was outlined by B.Hyde (Ottawa,Canada) and he stressed the importance of evaluating for this, if suspected, by thyroid ultrasound and needle biopsy despite normal serum thyroid chemistry.

Improvement in symptoms was reported in 6 out of 15 patients after administration of probiotics by A.Sullivan (Stockholm,Sweden). 8 patients were unchanged and one felt worse. Certain strains of lactic acid bacteria help to normalize the cytokine profile and have anti-oxidant effects.

SLEEP SESSION

An introductory overview of this session was given by J Shaver (Chicago,USA). Generally 1/3 of the population report poor sleep and are unrefreshed on waking. Sleep leads to mind/body recovery. There is no rule of thumb as to the amount of sleep needed, but the aim should be to function efficiently when awake. Sleep measurement was discussed, such as using self-report and polysomnography. Heart rate, leg movement and breathing could thus be monitored. Sleep can be affected by weak sleep drive, excess emotional or physiological arousal, poor synchrony of the light/dark cycle and negative sleep environmental conditioning. Therapy is aimed at: keeping attuned to the light/dark cycle; sleep restriction; behavioural cues, which include bedtime routine and avoiding incompatible cues and dampening of both cognitive arousal and physiological activation. She described various sleep disorders such as restless legs, periodic limb movement and breathing problems and also addressed issues relating to physical illness (such as CFS) and medication effects. Finally she mentioned that both growth hormone and prolactin release are lowered in fibromyalgia (FM), and the sleep disorders aforementioned are superimposed on the sleep deficit associated with FM.

C.Lapp (Charlotte NC, USA) followed with a further sleep overview from a physician's point of view. He emphasized that dealing with sleep is one of the most important aspects of the management of CFS. He described a number of problems associated with sleep in CFS: Non-restorative sleep, difficulty in intiating and maintaining sleep, restless legs syndrome (RLS), periodic limb movements (PLMs), nocturnal myoclonus, vivid nightmarish dreams, "tired but wired", phase shift and dysania (foggy,stiff and sore on waking). The sleep may also be affected

by primary sleep disorders (apnoea, periodic limb movements, narcolepsy) medication, FM, stress, depression and habituation. Sleep latency may also be increased and there maybe decreased sleep efficiency. In FM the sleep problems encountered include lowering of sleep efficiency and slow wave sleep, increased awakenings and K complexes in stage 2, and increased NREM α intrusion.

Lapp also described “Upper Airways Resistance Syndrome” (UARS), which is not as severe as apnoea, but leads to frequent arousal with slightly lowered oxygenation, more physical symptoms including low BP and mild eratic breathing. In one study of UARS, use of CPAP decreased physical symptoms by 40%.

The approach to treatment should be to rule out primary sleep disorders, deal with patient’s preconceptions and denials, emphasise sleep hygiene and consider CBT. Medication to be tried can include: melatonin, antihistamines and tricyclics. Dopamine agonists can be useful for PLMs and clonazepam can reduce restlessness and myoclonus. Reduction of pain is also an important issue. Non-restorative benzodiazepines, such as zopiclone should be avoided. Opiates will reduce short wave sleep and SSRIs may increase RLS. Alcohol should also be avoided.

SLEEP POSTERS

E.Van Hoof (Brussels,Belgium) found a number of sleep abnormalities as a result of a study in CFS patients. These include, sleep latency problems, α-delta intrusion associated with anxiety, but RnaseL-ratio did not correlate with α-delta patterns. The results therefore question RnaseL as a biological gradient.

It seems that CFS patients may have a heightened perception of sleep dysfunction compared with controls. M.Matthias (Atlanta, USA) found that reports of sleep problems were reported more often in patients than controls experiencing sleep disorders. There was a negative correlation between perceived poor sleep and reduced activity scores in CFS.

CLINICAL TRIALS SESSION.

This session began with 2 presentations by B Hurwitz (Miami,USA). He covered the previous research showing that those with CFS often have diminished RBC volume due to normochromic, normocytic anaemia (NNA). His team have studied the use of erythropoetin-α (EPO-α) on RBC volume, fatigue and susceptibility to syncope during head up tilt (HUT) in CFS patients. Patients whose ferritin levels were non responsive to iron supplementation were excluded. Of the 57 patients studied, 66.7% were found to have low blood volume of up to 15% below normal. They looked at the CRP and serum interleukin-6. Pro-inflammatory cytokines have a secondary effect in reducing RBC volume, due to probable suppression of RBC production in the bone marrow. Hurwitz concluded from this study that fatigue in CFS patients with low RBC volume was not improved by EPO treatment, but susceptibility to orthostatic syncope was diminished in those subjects with more substantive EOP-induced RBC volume improvement.

A preliminary trial by J Montoya et al (Stanford, USA) showed that Valganciclovir (over 6 months) was associated with positive clinical response in CFS patients with high antibody titres against HHV-6 and EBV. There was marked improvement in fatigue. This warrants a further double-blinded, placebo-controlled trial. This drug is active against all herpes viruses (including EBV and CMV) and is a well absorbed drug. There are potential haematological and renal side effects, and this drug should not be used in pregnancy.

M.Lerner (Michigan, USA) had also conducted a Phase 1 clinical trial using valaciclovir or valganciclovir or both for 6 months in CFS patients with positive EBV or CMV titres, who had abnormal ECG T wave flattening or inversion. All 37 patients treated had a positive response with

no serious side effects. However patients were encouraged to drink plentifully to avoid renal stone formation, and liver function tests and platelets were monitored.

CLINICAL TRIALS POSTERS

F.Garcia-Fructuoso (Barcelona,Spain) found modafinil effective in the treatment of daytime sleepiness in CFS. In a study of 31 patients, side effects were experienced by 67% and 5 patients (14%) withdrew from the study because of side effects. D.Blockmans (Leuven,Belgium) found that methylphenindate (2X10mg daily) was significantly better than placebo in reducing fatigue and concentration disturbance in a small % of CFS patients.

Lipid replacement and antioxidant therapy for restoration of mitochondrial functioning with a nutritional supplement (NT Factor) was found by G.Nicholson (Huntington Beach,USA) to significantly reduce moderate to severe fatigue.

T.Park (Seoul,Korea)used IV gammaglobulin 1gm weekly for 6 months coupled with strict diet (including increased salt), sleep (medicated) and exercise control and showed significant improvement in 50 CFS patients.

Advice for dental procedures was outlined by W.Saldana (New York,USA) and she stressed the importance of the dentist being part of the treatment team. Attention must be given to pain management, analgesia, and risks of oral bacteria.

R.Shoemaker (Pocomoke, USA) used low dose erythropoietin, in a short clinical trial, safely lowered symptoms and improved levels of C4a in responders. Maintenance of lowered C4a was associated with improved quality of life. Out of 60 patients, 51 noted symptom reduction, however 34 relapsed within 3 months. Another study suggested that the systemic inflammation in CFS caused by elevated C4a may be treated using erythropoietin and that the CNS correlates of cognitive dysfunction in CFS have an inflammatory basis.

In a further trial, Tadalafil was used in 30 CFS male patients. This drug has been shown to lower elevated pulmonary artery pressure. This usually falls in response to exercise, improving pulmonary venous return to the atrium. In the trial the drug was found to safely reduce dyspnoea and improved exercise tolerance concomitant with an improvement in pulmonary artery response to exercise. 93% had changes in erectile behaviour.

PAIN SESSION

Pain was described as a major feature in many aspects of CFS by K.Berkley (Tallahassee, USA) in her overview of pain. It can be extremely disabling, interfering with sleep and causing fatigue. Alleviating sleep disturbances can alleviate pain leading to improved quality of life. Patients conceptualise pain like touch, and better understanding of the mechanisms of pain can make a difference for the individual. There is a pain matrix in the brain and the experience of pain occurs as a result of central processing via a network in the CNS. Multi responses may occur in different organs. Constant integration of information from the body by the CNS leads to planning and reorganizing of body actions. Pain is not a pathway, but a dynamic process. Using endometriosis as an example, symptoms of muscle hyperalgesia, interstitial cystitis and irritable bowel syndrome may become more prominent due to the endometrial growths developing their own nerve supply and sending more input into the CNS leading to cross system interactions.

K.Kato (Stockholm, Sweden) looked at associations between chronic widespread pain and its co-morbidities, which included FM, CFS, IBS, etc in the general population. The associations are mediated by genetic and family environmental factors, and the extent of mediation via familial factors is likely to be disorder-specific. In these illnesses there are 2 latent distinct traits that` are common to all, but unique factors specific to each illness.

Mechanisms and treatment for fibromyalgia and related conditions was further expanded by D Clauw (Michigan, USA). He described FM as being caused by a combination of genetics, various triggers, and mechanisms such as the relationship between physiological and psychological factors, disordered sensory processing (e.g. increased sensitivity to noise, smell etc) and autonomic/neuroendocrine dysfunction. There is a strong familial disposition. FM patients can be categorized into 3 groups according to psychological factors. Those whose psychological factors worsen symptoms have more tenderness, high depression/anxiety, are high catastrophisisers and have no control over the pain. PET and fMRI have both identified a number of brain regions (thalamus, amygdala and prefrontal cortex) involved in pain processing.

There is good evidence to support the treatment of FM through education, aerobic exercise and CBT. Alternative therapies such as balneotherapy, hypnotherapy and biofeedback are moderately useful, but there is only weak evidence for use of other alternative approaches. There is strong evidence supporting the use of pharmacological agents such as tricyclics, SNRIs, and anticonvulsants, but doses should be increased very slowly. Tramadol and SSRIs are modestly helpful and there is only weak evidence to support the use of growth hormone, 5HTP, tropisetron or SAMe. There is no evidence for help from opioids, corticosteroids, NSAIDs, benzodiazepines, non-benzo hypnotics or guaifenesin.

PAIN POSTERS

A.Bested (Toronto, Canada) and A Logan (Harvard,USA) have written an excellent book "Hope and Help for CFS and FM" providing a useful tool for patients and professionals and covering a wide range of related topics. Sample copies were freely available.

EPIDEMIOLOGY and CASE DEFINITION SESSION

R.Herrell introduced the session by explaining the history and development of epidemiology and its application to study of disease in the 21st century. Use of modern statistical methods coupled with social and genetic epidemiology has furthered studies, identifying the aetiology of disease and determining interventions.

Epidemiological studies by W Reeves et al (Atlanta, USA) compared those meeting the current criteria for CFS, with those with fatigue but insufficient symptoms (ISF) to be diagnosed with CFS and non fatigued controls, in an attempt to subgroup those with CFS according to their level of impairment and symptom severity, and to see if persons with ISF do resemble any of the CFS subgroups. Results suggested that a subset of those with ISF do have a similarly severe illness to CFS, but usually without at least 4 of the case-defining symptoms.

A 10 year follow up by H.Kang (Washington, USA) of Gulf war veterans suffering from CFS compared to non-Gulf military peers, showed that the CFS symptoms decreased significantly in the Gulf compared to non-Gulf sufferers.

R.Underhill (New Jersey,USA) found that the offspring of mothers with CFS also risk developing CFS or CF in childhood or later life. CFS occurred in 5.5% 0f the offspring. Most of the offspring were born before the mothers developed CFS. 24% of the mothers had an offspring with CFS. Recovery rates were 50% for CFS and almost 1/3 for CF. 1/3 of the mothers also reported they had a parent with CFS or CF. There were however 5 times as many healthy offspring as fatigued. There were no other significant additional risks if the mothers had other blood relatives with CFS.

Monozygotic twin studies by A.Jacks (Stockholm, Sweden) using the non-affected twin as a case control, found that gene expression profiles can be explored efficiently. 35 pairs of twins discordant for CFS are being studied. Major co-variates such as depression, life events need to be considered, and full results of this important study should be available in 2008.

A follow-up from 9/11 looking at unidentified somatic complaints and coping strategies was undertaken by B.Melamid (New York, USA). This may provide an opportunity to look for early symptoms of unexplained illnesses such as CFS. There was no significant incidence of PTSD reported. Tendency to depression and substance and alcohol abuse were reported depending on proximity to site, loss of loved one etc. Coping with “hope” (less depressed) or “avoidance” (more depressed) were significant predictors of depression.

The economic impact of CFS on society in a community based versus tertiary based sample was discussed by L Jason (De Paul University, USA). In the USA there is a 27% reduction in employment attributable to CFS, with 19-27% receiving disability payments and 30% only able to work part-time. These indirect costs amount to about $17½ billion annually. The direct annual health costs for individuals in tertiary care are $8674 and in community care $2300. (This amounts to up to $7 billion annually). For non fatigued controls, annual health care costs $1132. The individual cost per person with CFS is equivalent to $25,000 annually.

The rates of CFS throughout the world are variable with an incidence in the USA of 2-4 per thousand. This is equivalent to 800,000 to 1 million people. L.Jason had also studied the rates of CFS in Nigeria, the first community based study in a developing country. Estimate of prevalence was 0.68%, and future research with larger studies is now needed. In Iceland, E.Lindal (Reykjavik) showed different prevalence rates of CFS according to the criteria used. The Fukuda criteria yielded a rate of 2.2%. There was no significant relationship between present day sufferers and those who were in the 1947 epidemic.

EPIDEMIOLOGY POSTER SESSION

Timed Loaded Standing (TLS) could be a useful measure in the study of populations reporting chronic fatigue. In a study reported by G.Moorkens (Antwerp, Belgium) major differences were shown between patients who were chronically fatigued in Belgium and the Gambia. TLS involves measuring the time a person can stand while holding a 2 pound dumb bell in each hand with the arms at 90 degrees of shoulder flexion.

J. Fernandez-Sola (Barcelona,Spain) found that 96% of patients diagnosed with MCS share the criteria for a diagnosis of CFS, and 25% also with that of FM. This suggests a common pathogenic mechanism.

T.Osoba (West of England) is working to produce a new case definition of CFS prevalence, to improve the sensitivity, specificity and accuracy of selection of CFS cases. L.Jason (DePaul University,USA) concludes that following use of a broad theoretically driven questionnaire, one can more accurately identify the critical symptoms in CFS. Whether or not to exclude other diseases and the degree of impairment experienced by various groups was the subject of the poster by J.Jones (Atlanta,USA). The contribution of fatiguing illnesses in general needs to be addressed as a public health issue.

B.Hyde (Ottawa,Canada) defined the illness in detail, outlining the course of the illness and those abnormalities which can be tested for. He outlined the advantages of the Canadian health system in allowing the physician the ability to order many technological tests at no expense to the patient. He outlined in a further presentation his longstanding historical involvement in CFS with visits to Iceland and Los Angeles.

BRAIN FUNCTION SESSION

The introductory overview was presented by G Lange (New Jersey,USA). She explained that the worse the results of tests of cognition, the worse the physical ability in CFS. Techniques for measurement included neuropsychological testing, brain imaging and spinal fluid analysis. These

could be static e.g. static MRI, showing white/grey abnormailites and brain volume, or dynamic. Examples of dynamic tests are SPECT (cerebral blood flow), CT (absolute and quantatitive blood flow), PET (bloodflow as base and during tasks, cerebral metabolism), MRS (concentration of brain metabolites) Blood O_2 Level-fMRI (non-invasive assessment of structure and function).

The abnormal findings in CFS were outlined:

1.Neuropsychological – abnormalities in: visual/memory, psychomotor function, attention span, information processing.

2.Static studies – Possible white matter loss, abnormal bright patches.

3.Dynamic studies – Reduced relative and absolute cerebral blood flow in lat frontal, med temporal, brainstem and ant cingulate areas. Reduced relative and cerebral metabolism of glucose and acetylcarnitine. Abnormalities in seratogenic transmitter systems, specifically in hippocampus and ant cingulated. Reduced 5HT and N-acetyl aspartate receptor binding potential. Elevated lactate. These dynamic studies are consistent. Those with CFS appear to perform cognitively as well as healthy controls, but use more brain areas than the healthy to achieve. Speed of information processing seems to be the key deficit.

4.Spinal fluid – Higher protein levels and all results greater in those without psycholoigical diagnoses. Elevated Il-8 and Il-10.

The work of the Spanish team headed by AM Garcia Quintana (Barcelona, Spain) was presented confirming abnormalities in cortical uptake, in all patients in the ant temporal and cingulate areas (prefrontal and inf frontal gyrus were also frequently involved), which correlated with elastase and RNaseL abnormalities in 38 patients. Information processing in CFS was shown to be prolonged in highly complex conditions by F.Togo (New Jersey, USA) after controlling for confounding variables. Depression had an additive effect in CFS, but does not explain the cognitive dysfunction in CFS. CFS patients have to work harder than healthy people to achieve same results.

J.Mark VanNess (Salt Lake City, USA) showed that CFS patients had slower reaction times compared to sedentary controls. This was compounded by 30 minutes exercise and 24 hours later, the CFS patients had definite persisting significant deficits. Occupational disability assessments need to include an exercise test and neurocognitive testing as validated by E Van Hoof (Brussels, Belgium).

The brain function session was summarized by H.Kuratsune (Osaka,Japan) with an overview of Japanese results. CFS has been shown to have an enormous economic impact in Japan costing the nation 10 billion$ annually. Their hypothesis is that neuro-molecular mechanisms lead to chronic fatigue. Brain dysfunction, metabolic abnormalities, reactivation of viruses, immunological abnormalities and HPA abnormalities are being studied. PET is found to be more sensitive than SPECT and have better spatial resolution. Brain acetylcarnitine uptake is abnormal in CFS, there is reduced binding power of 5HT in ant cingulate cortex (correlating with the pain score) and a number of abnormalities with reduced responsiveness on fMRI are an essential feature of CFS.

BRAIN FUNCTION POSTERS

J.Mark VanNess (Salt Lake City,USA) demonstrated significant metabolic abnormalities in CFS during exercise. There was consistent oxidative dysfunction, lower oxygen consumption and both peak and anaerobic threshold were down. There was no difference in glucose or lactate response. However RNaseL ratio and elastase activity failed to show any differences between the CFS patients and controls.

J.Alegre-Martin (Barcelona,Spain) showed there was decreased functional reserve and decreased aerobic power following an exercise test in CFS patients. Neuropsychological study also showed there was considerable cognitive deterioration, and a difference in processing between right and left hemispheres was also observed. There was an association between monocyte RNaseL and elastase suggesting involvement of elastase in the genesis of CFS and elastase inhibitors may have therapeutic implication.

That patients with CFS showed slowed cognitive and fine motor processing of visual stimuli leads to the consideration of psychomotor functioning being an interesting variable to consider in further neurobiological research, according to G. Moorkens (Antwerp, Belgium).

P.Cheney (Ashville,USA) found an 81% incidence of patent foramen ovale in CFS (normal 10-15%). The PFOs in CFS ca be modulated up and down supporting a defect in handling of oxygen by products in CFS similar to that seen in fetuses.

BEHAVIOURAL HEALTH SESSION

E.Stein (Calgary, Canada) gave an excellent overview of the behavioural health interventions in CFS published over the past 10 years. She described ME/CFS and FM as being chronic conditions requiring long term management, and although both have high rates of psychiatric comorbidity, neither is considered to be a psychiatric disorder. Because medications have not been shown to give significant benefit longterm, behavioural interventions have been considered relevant. Early CBT/GET models were based on the assumption that acute illness behaviours were causing or perpetuating CFS. But the only positive CBT study (defined by Fukuda criteria) was in adolescents. Some exercise studies have shown decrease in fatigue, but no studies have shown the effects of exercise or CBT on symptoms other than fatigue or general function. And no study has looked at the effects on the severely ill. In FM, less than half the studies using CBT/GET have resulted in improvements in pain, mood or health and by one year many of the effects have worn off.

Interventions in other types of chronic disease have different objectives and the Stanford model for self management is widely used. The aim is to help rather than treat or cure. The programme includes: exercise programme, cognitive symptom management, nutritional change, sleep and energy management, medication, community resources, emotional management, training of health care professionals. In a 2 year follow up for mixed chronic conditions, there was generalized improvement in self-rated health with reduced disability and fatigue. Self efficacy and acceptance of the illness are important. Suicide is the 3rd leading cause of death in CFS (others being cancer and heart disease) and “hope” based interventions for self management should include re-evaluation of life goals and priorities.

Medical education was the subject of a presentation by F.Friedberg (Stony Brook, USA).
31 fourth year medical students doing their psychiatry rotation attended a 90 minute seminar on the management of medically unexplained illnesses, exemplifying CFS and fibromyalgia. A modified version of the CFS Attitudes Test was administered before and after the seminar. A significant improvement in attitudes towards CFS was found, particularly in relation to favouring more federal funding for CFS research, employers providing flexible hours for those with CFS and disability issues associated with CFS. Even at initial assessment, the students felt it was important for physicians to understand CFS and that patients are not to blame for getting sick. This brief exposure to factual information about CFS and fibromyalgia was associated with more favourable attitudes towards CFS in fourth year medical students, and the encouraging discussion following presentation of this paper will hopefully lead to more input into medical education.

P.Fennell (New York,USA) discussed behavioural health with a CFS perspective. She noted that there has been a paradigm shift in medicine towards study of chronic illness. 1/3 of doctor visits

are for chronic illness, 2/3 deaths are caused by chronic illness and 78% of medical care expenditure is for chronic illness. There are 4 groups of chronically ill:
1. traditional (eg CFS, asthma, lupus)
2. Acute illness survivors (eg post-cancer)
3. Persistent acute illness (eg stroke, HIV)
4. Natural aging. Innovations in chronic care include health care corporations, pharmaceutical companies, federal government and chronic care models such as the Stanford model. The Fennell stage/phase based model is useful in CFS as illness changes over time and the patient needs to cope with change. Medical practice needs to be matched to the phase to improve compliance.

BEHAVIOURAL POSTERS

The Cog- health test is a short self administered computerized test sensitive to cognitive change and can be a useful tool is assessing cognitive function in CFS and related conditions. A. Cusco-Segarra (Barcelona,Spain) found that using this tool, cognitive function was impaired in CFS and MCS, but not in controls or FM.

C.Lennartson (Stockholm,Sweden) showed that low intensity training may be a safe start for physical activity without exacerbating symptoms in CFS. There were social and emotional benefits too.

The Four-Phase model was again described by P Fennell (New York, USA) as a tool for clinical case management to help improve coping, alleviate stress, enhance decision making and target interventions in CFS patients and caregivers. This approach can also be useful for victims of disaster. The four-phase model was also shown to be a useful adjunct to the model of human occupation (MOHO) by J.Burke (New York,USA) and can offer an effective treatment option.

The team headed by T.Matsui (Osaka, Japan) found that CFS patients are not as severely depressed with perfectionism traits as those with depression alone. But CFS patients were more anxious and showed more maladaptive coping behaviour than the depressed patients.

A small pilot study by J.Donalek (Chicago, USA) looking at the impact of CFS on the family with family experiences having to be reshaped, provided food for thought, and it is hoped this study will be enlarged. L.Till (de Paul, USA) describes a buddy system that could prove a useful support system for those with CFS, providing companionship and practical assistance.

D.J.Benet (Atlanta, USA) outlined an educational programme for primary care providers as a result of collaboration between government organizations and patient advocacy groups

There was a further intervention programme for medical students described by T.Lu (Loyola,USA). The aim is to assist future physicians with diagnosis and treatment of CFS as well as providing encouragement to see more patients with this illness. The trend in publishing of CFS literature over the past decade was reviewed by F.Friedberg (Stony Brook,USA). The output of peer reviewed CFS literature has not increased, but articles on FM and non-CFS fatigue have increased substantially.

Exercise intolerance in CFS is evident in a study by C.Ruud (Amsterdam, Netherlands). When CFS patients are subjected to increasing exercise, and compared to controls, there is a lower anaerobic threshold and a state of malaise comparable to overtraining.

Physical functioning was also shown to be improved in one woman by the daily IV infusion of 1L of 9% saline over 18 months. Cessation led to reduced function. L.Travis (Salt Lake City, USA) hypothesized that saline increased blood volume and/or augmented autonomic activity.

PAEDIATRIC SESSION

The paediatric session, introduced by L Jason (Chicago, USA) and D Bell (Lyndonville, USA) focused particularly on the new paediatric case definition, which has been produced by a working group over the past 6 months. For a diagnosis of paediatric CFS, the following 5 classic CFS symptom categories must occur: post-exertional malaise; unrefreshing sleep or sleep disturbance; myofascial pain, joint pain, abdominal pain and or head pain; two or more neurocognitive manifestations; and at least one symptom from two of the following three subcategories: 1. autonomic manifestations or 2. neuro-endocrine manifestations or 3. immune manifestations. The diagnosis can be made after 3 months of persistent or relapsing chronic fatigue that is not a result of exertion, is not substantially relieved by rest and results in substantial reduction in previous levels of educational, social and personal activities.

This new paediatric case definition should lead to more appropriate identification of children and adolescents with CFS. A paediatric health questionnaire has been produced with adult and child versions, to be filled out jointly by the child and/or caregiver.

Exclusionary criteria include past and present psychotic disorders of any variety, current anorexia or substance abuse. Treated depression is not exclusionary.

A panel discussion then followed focusing particularly on paediatric prognosis. D Bell (Lyndonville,USA) had done a 15 year follow up (from 1985) showing that 80% were “well” with 50% of these normal and 50% well but leading limited lives. 20% were still considerably impaired. K.Rowe (Melbourne, Australia) found 60% well at 5 years, 20% nearly better and 20% at about 50% normal. In Japan 75% were described as well at 5 years by T.Miike (Kumamoto,Japan).

A paper then presented by K Rowe (Melbourne, Australia) found that of 87 young women at a Melbourne adolescent CFS clinic, 61% had complained of debilitating pain during menstruation, compared to 40% of recovered patients. A 3 month study on 7 young women confirmed significant worsening of CFS symptoms associated with their severe dysmenorrhoea. All responded well to treatment with a combined oral contraceptive pill following an unsatisfactory trial of non steroidal anti-inflammatory medication. Subsequently 56 young women have responded well to oral contraceptives, mostly used continually, with relief of symptoms and improvement in functioning with regard to CFS. This raises the hypothesis that inflammatory cytokines from the uterus may exacerbate CFS symptoms in conjunction with dysmenorrhoea.

A study of perception of social environment by adolescents with CFS particularly in relation to school was described by E Van Hoof (Brussels, Belgium). 52% of 27 adolescents with CFS reported conflicts at school, 22% attended school fulltime, 82% had stopped some courses. 48% reported having few friends. She stressed that the diagnosis should be considered as early as 1 month after onset, and this study showed an average of 18 months before a diagnosis was made.

C Van der Eb (Lake Bluff, USA) described an adolescent self management protocol, which showed promise as a strategy to help adolescents with CFS to adjust activity/rest and cognition to facilitate symptom management and be more able to participate in normal teenage pursuits.

PAEDIATRIC POSTERS

No link could be confirmed between the putative symptoms of “hypoglycaemia” and documented blood sugar levels, according to research by F.Cameron (Melbourne,Australia). A number of symptoms maybe attributed to a diagnosis of “hypoglycaemia’, but special diets are not likely to be of benefit therefore.

E.Van Hoof (Brussels,Belgium) said that as skepticism is often associated with a diagnosis of CFS, parents maybe accused of neglect or abuse. A case study indicating the mistrust and

dismissal experienced by some families illustrated this and tragically Munchausen by proxy can be mistakenly diagnosed.

GENDER ASPECTS of CFS SESSION

B.Evengard (Stockholm,Sweden) gave an overview of gender health. She discussed 3 aspects: Reproductive health (eg breast and prostate cancers); biological differences (eg myocardial infarction) and gender neutral diseases (eg psoriasis) However in gender-neutral diseases treatment can be gender-different. She cited the management of psoriasis in a hospital clinic where treatment was quite different for the sexes with females getting more creams and males more phototherapy.
IN CFS more females than males get this illness, and this could be a biological difference or a social (gender) difference. Gender is a social construct. In research men and women should be divided and study design reconsidered. She finished by quoting a Mr Trevis: "It is unethical, unintelligent and uneconomical not to work with gender issues".

Gender, sexuality and intimacy are secondary to the clinical encounter in CFS patients according to P Fennell (New York, USA), but should be given equal weight. They can adversely affect assessment and treatment. The illness may affect the mechanics of sex – exertion, libido and psychological aspects are all involved. Sexual relationships do change over time and in an illness such as this, patients may need to learn to touch again, to achieve fulfillment.

Addressing issues based on gender were further reiterated by L Bateman (Salt Lake City, USA). For women, chronic illness is generally more common and women may not be taken as seriously as men. However thinking of CFS as a "women's" disease may delay men seeking help for CFS. Coping styles may vary between men and women and both male and female spouses carry a heavy burden in many ways. Intimacy issues and issues associated with disability insurance may be different.

In the area of research, gender differences may affect test results and disease process, and choice of case definition may affect gender demographics and alter generalizations made about gender. Comorbid mood states, coping behaviours and stress factors may vary by gender as well as subgroup. HPA axis, autonomic nervous system and immune function are affected by gender in complex ways and there is little gender-specific CFS research. By being more aware of gender issues, better clinical care maybe possible together with better understanding of this illness.

GENDER POSTERS

2 studies were presented by C.Javierre (Barcelona,Spain) and concluded that in a large group of women compared to healthy female controls, those affected by CFS showed a worse response with lower efficiency to light intensity exercise. Reduced ventilatory efficiency in CFS maybe responsible for a lower PCO_2 in blood, associated with weakness and post exertional distress.

CARDIOVASCULAR PRESENTATIONS

A.Suarez (Barcelona,Spain) looked at cardioventilatory response in a group of 135 CFS women compared to healthy controls. The control group scored 52% higher with workload in maximal test, with O_2 uptake 47.5% higher. However in a further supramaximal test after a 5 minute rest, the CFS subjects were able to increase their responses considerably.

Diastolic dysfunction in CFS patients is reported at a level well above that for control populations of the same age according to P.Cheney (Ashville, USA). This supports the hypothesis that CFS is a syndrome of cellular energy deficiency. Tilt-echocardiography provides amplification of often masked diastolic dysfunction in patients known to be sensitive to head-up tilt. He cited the possibility of an associated cardiomyopathy as previously described by Natelson and Peckerman.

V.Spence (Dundee, Scotland) showed that CFS patients have significantly increased levels of plasma hs-CRP, $F_{2\alpha}$ isoprostanes and oxLDL that correlate positively with arterial stiffness. CRP was a strong predictor of arterial stiffness conferring a significantly increased risk of a future cardiovascular event in CFS patients.

GENETICS/PROTEOMICS SESSION

A summary of the current state of genomic science relating to CFS was presented by S.Vernon (Atlanta,USA). Genetics is the study of the genes and genomics covers the function and interactions of all the genetic material in the genome. Biologic samples for these studies can be blood, saliva and urine. The analysis includes classical statistics, data mining and pattern recognition, machine learning and multidimensional approaches. Data integration refers to the integration of different types of data and differential analysis techniques.
The focus should be on the blood, with 5 litres circulating and blood cells being the sentinels of the disease process. The plasma also has proteins from throughout the whole body. There is dynamic traffic between the blood and the brain.
Genomic technology involves profiling by micro-array, gene chips, reverse transcriptase-PCR. Mass spectroscopy is used for protein. Differentially expressed genes are not always the same in various studies, but there is overlapping of pathways and correlation with CFS symptoms. It is possible to subtype CFS genetically.
By using gene technology, it is possible to understand who may develop an illness. Genes may also serve as biomarkers, and pharmacogenetics can lead to treatment.

F.J.Garcia-Fructuoso (Barcelona, Spain) was unable to present his work in this field owing to illness, but his team emphasise that CFS and FM are 2 genetically distinguishable illnesses, with CFS being an exclusion diagnosis for FM.

A fascinating study using the Utah Population Data Base to explore a genetic contribution to CFS and associated disorders was presented by F.Albright (Salt Lake City,USA). They used 3 techniques looking at risks for CFS in relatives, relatedness among CFS patients and identification of high risk CFS pedigrees. First degree relatives share many environmental risks and exposures (relative risk 7.68); but in second degree relatives this is less of a factor (relative risk 2.54). This suggests a genetic component. It is hoped this study will lead to gene identification predisposing to CFS and related conditions.

The sex difference observed in CFS indicates a role for oestrogen and oestrogen receptors for disease development and this issue was addressed by B.Evangard (Stockholm, Sweden). Reduced ERbetawt expression is consistent with an immune mediated pathogenesis of CFS. She said that a possible connection between oestrogen, oestrogen receptors and CFS needs to be further evaluated, particularly as estradiol and progestin improve health status in CFS and there is also improvement in pregnancy.

J.Baruniuk (Washington DC, USA) obtained genetic samples from the cerebrospinal fluid of 52 patients with CFS, FM and GWI and compared with healthy controls. 5 proteins were predictive of CFS and were absent in the healthy controls. The specific CFS-related proteome suggests a common pathophysiology for these related illnesses, and detection of at least one of the proteins is predictive of CFS.

However the research presented by E.Aslakson (Atlanta,USA) showed that a more complete enumeration of altered pathways demonstrated distinct and differing altered biological pathways among CFS subjects, further demonstrating the heterogeneity of CFS.

J.Kerr (London,UK) outlined his team's research. The precise gene signature and metabolic pathways need to be identified. The utility of genomics/proteomics can involve inheritance,

pathogenesis and diagnosis. Molecules of interest include DNA, RNA and proteins and there is potential for future study of lipids and glycans. Predispositional genes for CFS have been identified associated with Q fever and parvovirus B19. Micro-array techniques are used and immune response, several mitochondrial genes and gene protein signalling are considered important.
Studies include:
1.TNFα found to be elevated in subgroups of CFS. Etaneacept is a potential treatment.
2. Cerebrospinal fluid proteome. Proton MRS of brain.
3. Urinary excretion of GABA.
4. Serum analysis using new infra-red spectroscopy. This could lead to a diagnostic test.
5. Infection is known to be important, so 28 possible microbes are being studied.
Kerr emphasized that this illness is a result of psycho-neuro-endocrine-immune interaction.

GENETICS/PROTEOMICS POSTERS

S.Mangalathu (Atlanta,USA) described sequence variations in certain genes involved in the regulation of the HPA axis and seratonergic system associated with CFS, allostatic load index and particularly with a CFS subgroup characterized by low HR variability and low urinary free cortisol. These tests need further validation with larger sample size.

R.Petty (London,UK) hypothesised that CFS patients may exhibit a miRNA gene signature and tested this by microarray in 15 CFS patients compared to healthy controls. It is hoped that knowledge of the miRNA gene signature of CFS will aid our understanding of the pathogenesis and lead to treatment development. This team, headed by J.Kerr are close to final details.

Significantly differentially expressed genes have been identified in a female patient group with gradual illness onset and no previously documented infection. This work presented by H.Grans (Stockholm,Sweden) stressed the importance of subgrouping CFS patients.

G.McKeown Eyssen (Toronto,Canada) postulated that impaired metabolism of toxic chemicals maybe the mechanism underlying MCS. A genetic predisposition for MCS may involve altered biotransformation of environmental chemicals. A gene-gene interaction between CYP2D6 and NAT2 (common polymorphisms) suggests that rapid metabolism for both enzymes may confer substantially elevated risk.

B.Burke (London,UK) investigated human gene signatures of past persistent microbial infections in unstressed normal blood donors, to consider possible relevance to the pathogenesis of CFS. This work may provide insight into the role of persistent and pre-existent infections in the pathogenesis of subsequent disease development.

NEW METHODS FOR EVALUATING FATIGUE SESSION

This session was coordinated by the Japanese Association for Fatigue Sciences. The first presentation was given by A.Sakudo (Osaka,Japan) showing that Vis-NIR spectroscopy (a non-invasive technique) for sera combined with chemometric analysis is a promising tool to objectively diagnose CFS.

T.Sugino (Wakayama,Japan) discussed the reactivation of HHV-6 and HHV-7 in saliva during fatigue states. Reactivation of HHV-6 relates to extra work load in CFS, while reactivation of HHV-7 relates to the actual fatigue state in CFS. These viruses have lifelong latency and HHV-6 establishes complete latency in peripheral blood macrophages, and when reactivated is shed directly into the saliva. Reactivated HHV-7 is amplified in peripheral T cells. Virus shedding is influenced by immunological status.

Application of DNA chip for fatigue assessment was outlined by K.Rokutan (Tokushima, Japan). Only 2.5ml of blood is required for samples. 9 CFS genes have been identified by PCR and micro-array. The identified genes may be important for subgrouping CFS.

Several of the Japanese researchers mentioned an anti-fatigue substance prescribed in Japan. This was D-Ribose.

VIRAL & IMMUNE INTERACTIONS and HEALTH SESSION

Symptoms observed in CFS are compatible with viral aetiology, and it is possible that CFS is associated with endogenous latent viruses. This was the basis of the talk by R.Glaser (Ohio, USA). Psychological stress is implicated in CFS, which in turn can modulate the expression of several latent herpes viruses including EBV. It has been shown too that the immune and endocrine systems "talk" to each other via receptors. Latent viruses such as EBV and HHV-6 may induce immunopathology by synthesizing viral protein in latently infected cells or in cells in which the virus genome is only partially expressed. These proteins could then induce immune dysregulation with effects on cytokines and chemokynes and/or T cell or NK function. It is difficult to link a specific virus to CFS if the viral reactivation is incomplete, as virus DNA would not be synthesized. Glaser's team have shown that EBV encoded dUTPase is able to induce immune dysregulation and associated symptoms in mice. This suggests that at least one protein of the EBV early antigen complex can induce immune regulation and maybe involved in the pathology of EBV-associated disease.

Also from Ohio, M.Wiliams discussed the issue that HHV-6 U45 protein is not a functional dUTPase, but it does induce immune dysregulation similar to EBV-encoded dUTPase.

D Ablashi (Santa Barbara, USA) described assays that can now be used to detect chronic reactivation of HHV-6 and EBV. It is vital to be able to distinguish between chronic, active and latent infection with these viruses. Studies have shown that there is a positive association between active HHV-6 and EBV and CFS. Many viruses could be implicated. RNase-L was also found to correlate with HHV-6 infection in CFS (67% concordance).
The possibility of antiviral agents being effective was discussed. Cidofovir, foscanet, ganciclovir and valgancoclovir all have potential. Studies with acyclovir have proved negative, but both ampligen and isoprinosine can be useful. Amantadine, red-mauve algae and lamotrigine have all shown promise in vitro.

GWI and CFS were compared immunologically by M.Fletcher (Miami, USA). Perforin is a molecule in cytotoxic lymphocytes necessary for killing and is found to be low in both illnesses. NK cell function is low in GWI and moderately low in CFS. CD2 and CD26 activation is high in GWI and moderate in CFS. CD26 cleaves neuropeptide-Y (NPY) and there is significantly reduced NPY in the plasma in GWI but not significantly in CFS. Further studies are underway.

B.Gurbaxani (Atlanta,USA) detected elevated Il-6 in the resting state in CFS patients (compared to controls) suggesting that proinflammatory cytokines could be contributing to symptoms – and a potential cause or effect of CFS. Il-6 correlates well with CRP and has a negative correlation with cortisol.

The incidence of HHV-6 and EBV infection in CFS was further discussed by S.Levine (New York, USA). Their team tried to determine if there were biologic markers of active, chronic viral infection in CFS patients compared to healthy controls. Evidence suggests that there is a subset of CFS patients suffering from these infections. Quantitative PCR in plasma is not useful as there is very little free virus in the plasma, and neither is PCR in PBMCs without a threshold, as it detects both latent and active virus. However serological assays (IgG to HHV-6 and EBV early antigen) are useful as long as a high threshold is used.

M.Murovska (Riga,Latvia) presented results of a study in Latvia of CFS and a possible association with HHV-6 and HHV-7 infection. This study also included symptomatology and occupation of patients. She had found that the rate of CFS morbidity is associated with professional activity and amount of intellectual work. Both viruses may be involved in the aetiology of CFS and reactivation may provoke immunodysfunction.

Because many CFS patients have persistent or intermittent gastrointestinal symptoms, J.Chia (Lomita, USA) evaluated the presence of viral capsid protein-1 (VP1) and enteroviral RNA in stomach biopsies. These were detected in a number of the biopsies of CFS patients with chronic abdominal complaints, compared to none in controls.

G.Nicholson (Huntington Beach, USA) discussed the chronic bacterial co-infections found in CFS. These included evidence of high incidence of systemic mycoplasmal infections of various types and a tendency for those with multiple infections to have more symptoms. Lyme disease, rickettsia and protozoal infections could all be implicated. The ticks causing transmission of Lyme disease may transmit a wide range of infections as well as B.burgdorferi, including mycoplasma, bartonella and ehlicia.

This whole session was summarized by A.Komaroff (Harvard, USA). He reviewed the immune abnormalities which have been demonstrated in CFS. These include activated CD8 (T cells), poorly functioning NK cells, abnormalities in the 2-5A pathway (RNaseL ratio), cytokine abnormalities (proinflammatory dysregulation), increased TGFβ and 27 times more circulating immune complexes than in controls. Many infectious agents have been cited as implicated such as EBV, Lyme, parvovirus, enteroviruses, Q fever, RRV, mycoplasma, HHV-6 etc. There is evidence for reactivation of HHV-6 and EBV, although the case is not entirely solid as yet. HHV-6 has been shown to infect neural and glial cells and persist in the CNS. It can cause encephalopathy and demyelination and is associated with MS and possibly seizures and cerebral palsy, although these are provocative studies. It is important to distinguish the active from the latent forms.
Over the past 10 years there has been increasing evidence that infection is most likely to be a prime cause of CFS.

VIRAL/IMMUNE POSTERS

A national ME observatory with funding from lottery is being established in the UK. D.Pheby (London,UK) outlined the proposal and they will include various research studies with a vision of advancing science.

J.Mikovits (Incline Village, USA) looked at HHV-6 and its intergration into host cells, and this study will contribute to an understanding of whether this virus contributes to CFS, malignancy and immunodeficiency associated with these conditions. Of 40 patients studied, 3 were positive to CIHHV-6.

A.Vojdani (Los Angeles,USA) stressed the importance of screening for Lyme disease and other related disorders due to overlapping symptoms. In vivo-Induced Antigen Technology is a new technique described which identifies pathogen antigens that are immunogenic and expressed in vivo during human infection.

Cryptostrongylus Pulmoni is a worm found in the sputum of 63% of CFS patients in a study by L.Klapow (Santa Rosa, USA). Retention of infected larvae leading to chronic auto-infection is a possibility in CFS. Larvae could also migrate from the intestines and back into the lungs. If this is occurring, inhaled anti-roundworm medications would seem logical.

N.Klimas (Miami, USA) reported a dramatic significant increase in the number of NK cells (X4) in peripheral blood following an exercise challenge in GWI. T cells also increased (X1.5), and both

sets of cells had returned to baseline at 4 hour follow up. There was no significant effect of the exercise on the actual percentage of activated T cells and NK cells or in the number of molecules per NK cells.

Visible and near-infrared spectroscopy was used by Y.Hakariyal (Osaka, Japan) for diagnosis of SLE with fatigue similar to CFS. SLE was detected in 85.7% SLE patients, and differentiated between anti-phospholipid (aPL) positive and negative patients. CFS can be discriminated from SLE and aPL.

B.Evangard (Stockholm, Sweden) compared the composition of intestinal microflora in CFS patients when in the acute phase of the illness. Increased levels of c.albicans were found and may prove a useful marker for ecological disturbance and contribute to symptoms. Future research is thus warranted.

Chronic enteroviral infection may be implicated in the cause of CFS. J.Chia (Lomita, USA) postulated that further viral studies could lead to the use of antiviral agents directed against viral RNA polymerase. Their team showed there was improvement in symptoms in EV positive CFS patients treated with α-interferon and ribavirin or combined α- and γ-interferon.

D.Strayer (Philadelphia, USA) did a meta-analysis of 2 trials of ampligen and found it was generally well tolerated in CFS and provided significant improvement in exercise duration and concomitant medication usage when compared to placebo.

Active infection with CMV maybe detected in patients with life-altering fatigue and this maybe useful guidance in making a diagnosis and use of antiviral treatment. M.Lerner (Detroit, USA) described use of IgM serum antibodies to CMV nonstructural gene products p52 and CM2.

Data produced in one study to check cytokine patterns in CFS did not support a Th2 cytokine bias. S.Repka-Ramirez (Utah,USA) did a study using nasal lavage to check mucosal immunity and eosinophilia to test their hypothesis.

Comparing CFS patients, FM patients and controls by L.Bazzichi (Pisa, Italy) looking at antipolymer antibody seroreactivity, it was shown that seroreactivity was higher in CFS than FM or controls. Cytokine levels were not significantly different between CFS and FM.

The whole conference was finally summarized by Prof Anthony Komaroff and he is encouraged by the wealth of new research presented and the exciting developments we have seen in the understanding of this illness over the past decade. The future certainly bodes well for CFS. Dr Klimas was thanked for her hard work in bringing such an excellent conference together, and members of the IACFS were encouraged to vote towards a name change for the organization to the International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyopathy – quite a mouthful, but a true reflection of the organisation's international status and more acceptable options for the name of the illness.

I must thank the ANZMES for their help in enabling me to attend this very worthwhile event.

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