THE 9th INTERNATIONAL IACFS/ME RESEARCH AND CLINICAL CONFERENCE

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Summary by Rosamund Vallings, M.B., B.S.

I was privileged to attend the IACFS/ME 9th International Research and Clinical conference from 12-15th March, 2009 in Reno, Nevada. Attendees from all around the globe were present and much lively discussion ensued following the papers presenting the latest cutting-edge research.

The main conference opened with an invited lecture from Yasuyoshi Watanabe (Osaka,Japan). He spoke on the importance of Fatigue Science for Human Health. He told us that fatigue is an important bio-alarm, without which we might lapse into unrecoverable exhaustion, or even die. Fatigue is strongly correlated with motivation. Fatigue decreases efficiency, and scientists are extensively analyzing the causes of fatigue, looking at therapy to aid recovery and preventative strategies. Of fatigue related illness, 30% suffer from Chronic Fatigue Syndrome in Japan, of which 1.3% are children. Other main causes of fatigue are other organic illnesses (28%), mental illness (30%), drug side effects and the effects of surgery. The Japanese have developed a new questionnaire and a fatigue scale. Much research is occurring in Japan with the development of large new centres.

Dr Watanabe then focused on CFS, discussing potential immune, biochemical and endocrine biomarkers. Plethysmography, visible and near infra-red markers for analysis of serum samples, gene expression and APISST (which relates to cytokine signals) are all being researched. HHV6 has been found to be physiologically increased in saliva after hard work, with levels improving after holidays. There are increases in HHV7 also after hard work and slightly less so in CFS. HHV6 is directly shed into the saliva, while HHV7 is amplified in the peripheral T cells. Brain function is studied using PET, functional MRI and MEG. Areas of the brain associated with fatigue, pain and attention have been demonstrated. Other CNS abnormalities include: abnormal acetylcarnitine levels in PET scans, reduced binding potential of 5HTT, mood changes shown to relate to the dopamine system, visual task activity lower in CFS on fMRI, and on MRI morphometry, there was volume reduction in the prefrontal cortices. This latter finding may relate to cortical plasticity, as it improves with CBT.

Work with animal models was discussed, looking at physical and mental fatigue, infections and complex tasks. In general there was shortage of energy for repair, changes in genes and amino acid changes with fatigue.

Session 1

Pharmacologic and Non-pharmacologic Treatment Advances

The first paper was presented by Greta Moorkens (Antwerp,Belgium) and was focused on their studies using combined CBT and Graded Exercise. 180 CFS patients were studied and a number of onset triggers were identified, together with co-morbidity factors such as depression, busy lifestyle and violence. Patients and staff reported some personal benefits, but statistical analysis did not show any significant improvement with combined CBT and graded exercise, and this negative outline warrants further research. Recommendations were that GPs needed help with suitable interventions via specialist expert advice.

Elke van Hoof (Brussels, Belgium) had looked at the influence of EMDR (eye movement desensitization and processing) and biofeedback on the hypervigilance in CFS. EMDR reduces amygdala reactivation. Patients were given 4 sessions of EMDR and followed up 4 weeks later. There were no significant differences in heart rate variability, but a positive trend was evident. All patients however improved in physical functioning significantly in areas of vitality, fatigue and concentration. They reported

feeling more insight, more control and were enthusiastic about this approach. There is need to look at the protocol further and also deal thoroughly with other life stresses to get the maximum benefit.

Nicole Porter (Chicago, USA) reviewed some alternative medical interventions in the management of ME/CFS and fibromyalgia. She found that several modalities have potential for future clinical research. A limited number of studies have been done with often suspect methodological quality. Few studies have been done looking at laboratory outcomes of immune function, and there have been inconsistencies of assessment instruments. There is a lack of randomized trials and a lack of reporting of negative results. The strongest evidence for treatments of useful value were in the cases of acupuncture and meditation. There is great research potential for looking at supplements such as carnitine, magnesium and S-adenosylmethionine. Qigong may also be helpful, but studies have lacked controls.

Interferon and cytokine levels in the phase III trial of Poly I: Poly $C_{12}U$ (Ampligen) was presented by David Strayer (Philadelphia, USA). Pre-treatment and intra-patient changes from baseline were compared to see if the treatment had a significant effect on serum levels. Patients had improved significantly in treadmill tests and decreased use of other medications with this treatment, but there was no significant modulation of interferons or cytokines. No safety concerns were raised and the treatment was well tolerated. The decrease in use of concomitant medications was an important point, as several of the medications used regularly in CFS do cause prolongation of the QT interval, with possible risk of death. Overall death rates in CFS patients due to heart failure, suicide and cancer were reduced.

The patients' own experience of living with post-infectious fatigue syndrome (PIFS) following an GI infection caused by Giardia lamblia in 2004 – Eva Stormorken – (Vaaler, Norway) – Preliminary findings from a qualitative interview study suggest that all the participants were healthy pre-giardiasis and were either working or studying on a full time basis. Four years later the mean functional level was still below 50% compared with pre-illness functional level, and none were able to either study or work on a full time basis. Findings also suggest that PIFS affects all aspects of life, including disrupted partnership and identity, and loss of friends, leisure activities, as well as work or education. In addition, most of the interviewees reported difficult encounters with health personnel who lacked. Both physical and cognitive complaints varied in number and severity.

Cognitive behavioural therapy was looked at from a patient perspective by Elke van Hoof (Brussels, Belgium). 96% of the 100 patients studied were motivated when starting CBT. 25% were using parallel medical treatments. Only 2% of those studied reported total recovery, and 30% mentioned some improvement. 30% reported no change and 38% were worsened. Only 25% were able to complete the programme, due to the physical component. Results of this study do not confirm effectiveness of CBT for ME/CFS, and large scale application is not supported.

CBT was reframed by Michael Antoni (Miami, USA), and he hypothesized that chronic stress influencing the HPA axis may influence the severity of CFS via changes in the pro-inflammatory cytokines. A cognitive behavioural stress management programme (CBSM) was devised using a telephonically designed programme (T-CBSM), after earlier success with group programmes. Participants received 12 weekly sessions via a phone link. Muscle relaxation, imagery, autogenic training, meditation and breathing exercises were included. Controls received a series of health education modules also by phone link. Pain, cognition and sleep symptoms all improved in the T-CBSM group and reduction in Il-6 equated with symptom reduction.

Patricia Fennell (Albany,USA) addressed the role of trauma experiences causing increased stress, which needs to be considered in chronic health management. Trauma may be disease/syndrome related, iatrogenic, cultural, vicarious, pre-morbid or co-morbid. Trauma is not a steady state and effects may wax and wane. In CFS, disability issues can provide added stress/trauma. The Fennell Four phase model can be an effective method for assessing and treating illness-induced trauma.

The clinical and immuno-modulatory effects of Isoprinosine were discussed in a paper presented by Maria Vera, (Miami, USA). 61 patients fulfilled the criteria for inclusion in this study. Patients were treated with Isoprinosine 500/1000mg (odd/even weeks) 3 times a day from Monday to Friday for 6 months. Clinical and immunological assessments were made pre-treatment and post therapy. There was highly significant improvement in the clinical scores of patients treated with this

drug at 6 and 12 month follow up. CD4+CD38 T cells were normalizing at 6 and 12 months, NK cell activity was improved and EBV titres had a highly significant decrease after 6 months. No patients developed gout (a recognized side effect) but 26% did experience gastro-intestinal symptoms. A larger randomized trial would seem appropriate. The downside is that this is a very expensive drug.

Session 2

New Developments in Epidemiology

Causes of death in 36 patients with CFS was compared to deaths in non-CFS patients by Rosamund Vallings, (Manukau, NZ). Causes of death in CFS patients did not differ from non-CFS patients or NZ norms apart from a higher rate of accidental deaths. It is probable that CFS patients can easily tire and overdo physical and mental activities, putting them at greater accident risk. Risks of late diagnosis of cancers were addressed, with a warning to make sure patients do report new symptoms and attend for regular screening.

Tokuzo Matsui (Osaka, Japan) reported the need to revise the exclusion criteria for mental health disorders in order for a diagnosis of CFS. The number of CFS patients diagnosed initially by the 1992 definition increased by 10% when the Japanese 2007 guidelines were used. Anners Lerdal (Drammen,Norway) also found that mental stress, such as PTSD symptoms are strongly associated with fatigue. Using multivariate analyses, demographic variables, mental stress, somatic conditions and self rated health all made significant contributions.

Further work from the Dubbo Infection Outcomes Study was presented by Andrew Lloyd (Sydney, Australia). Q fever is a zoonotic illness caused by Coxiella burnetii infection. Some patients suffer long term serious disability. Prolonged symptoms of post-infective fatigue were associated with more severe illness, but not with persistence of the genomes of the infecting organism in peripheral blood cells, alterations in immune responses or changes in the proportions of immune cell subsets. The importance of prospective studies was stressed.

Eliana Lacerda (London,UK) had looked at work related risk factors for chronic fatigue. Bank workers in Brazil were the subjects of this study. Fatigue and Chronic Fatigue in this group were strongly associated with RSI. Ergonomic variables were also important determinants of CFS/ME like syndrome. Looking at preventative measures in the work place seems essential, and also paying attention to such issues as breathing, posture and adequate organizational structures.

Roumiana Boneva (Atlanta, USA) found that in a community study, a positive gynaecological history, such as early menopause, hysterectomy, oophorectomy etc may be associated with CFS. The patients had more irregular periods than controls, more births, and pain associated endometriosis. 53% had had a hysterectomy compared to 40% of controls, 37% had had a D&C compared to 11% of controls. She recommends a larger study.

Classification of persons with ME/CFS by types of fatigue was a useful study by Aaron Boulton (Chicago,USA). Important subgroups emerged, and it is possible that the fatigue patterns in these people may represent different subtypes. The fatigue patterns are heterogeneous, and future research needs to focus on this.

Session 3

Neuro-endocrine Advances

A.Suárez (Barcelona,Spain) suggested that the measurement of hormonal values in CFS patients could help with diagnosis. There were no significant differences in ACTH parameters, but those with CFS had significant lowering of cortisol levels on the 3 days of exercise challenge testing. The differences in prolactin and growth hormone were not significantly different to controls.

Patients with fibromyalgia and/or CFS demonstrate sustained increases in gene expression for metabolite sensing receptors

and βadrenergic receptors on leucocytes from 0.5 to 48 hours after exercise. This is the time when pain and fatigue worsen, even when muscles are inactive. This study by Alan Light (Utah, USA) suggests a predisposition for these receptors to increase dramatically after exercise, stress and infection. There is potential for the increases in gene expression to provide biomarkers.

Mary Ann Fletcher (Miami, USA) found that Neuropeptide Y (NPY) correlates with symptom severity in CFS. NPY was elevated in CFS compared to controls (p=.001) though there was some overlap between controls and CFS. This could be used as an assay to correlate with severity of illness, particularly in relation to psychological symptoms. NPY may be a potential biomarker for CFS and may be an important mediator of the illness itself, thus it is a target for therapeutic strategies. But for now it needs to be combined with other potential biomarkers such as gene expression. NPY needs radio-active assay and cheaper methods need to be developed.

Jonathan Kerr (London,UK) discussed the impact of stress on the likelihood of developing CFS following Parvovirus B19 infection using negative life events, perceived stress and negative affect. 5 of 39 cases developed CFS and 4 of the 5 were viraemic at follow up. Stress index was significantly associated with the development of fatigue during the acute phase of illness, and also with chronic fatigue and arthritis in the 3 years following the acute B19 infection. Statistically it was found that a high stress index was the primary predictor of CFS/ME 1-3 years following the initial infection. Of the 5 cases followed, IV immunoglobulin therapy for B19 gave benefit, with 3 patients recovering completely. 2 withdrew because of headaches. 400mg.kg/day was given IV for 5 days.

The immunomodulatory effects of sodium oxybate in patients with α-wave intrusion during deep sleep was studied by Natalie Hone (Miami, USA). The average dose was 6.1gm daily. The study revealed a high rate of sleep disorders in CFS patients. α intrusion was the most common disorder, more so in women than men. 45.9% of patients had sleep apnoea (males more than females). Sodium oxybate had no significant immunomodulatory effects in patients with α intrusion, but sleep improved markedly clinically.

Session 4

Infectious Diseases Research

Kenny de Meirleir (Brussels, Belgium) opened this session with an overview of his research looking at herpes virus and parvovirus B19 DNA in the gastric and intestinal mucosa of patients with CFS. HHV7 was frequently found in both patients and controls. EBV and HHV6 were also detected in patients and controls, and HHV6 was detected significantly in a small subset of patients in duodenum and stomach. However, parvovirus B19-DNA was detected significantly more frequently in the stomach of patients more frequently than controls, and B19 DNA was found in the peripheral blood of those biopsy-positive patients. One case study of a 20 year old female (+ve B19) was treated for 4 months with γ globulin and there was no residual load of B19.

Viral gene micro-array was used to detect viral DNA in 40 patients by the team led by Judy Mikovits (Reno,USA). 1608 viral transcripts, microRNA or endogenous viral elements were observed in the subgroups of patients and controls. Adeno- and rhino-viruses were the most commonly detected in the controls. Herpes viruses (particularly HHV7 and CMV) predominated among the CFS patients. Human endogenous retroviral elements were also differentially expressed. This may be significant in CFS as neuro-degeneration can result. Bombyx mori densovirus was the 5th most highly expressed virus in CFS patients, and adeno-associated-virus 3,3e,4 and 2 were all in the top 20expressed in patients but not in the controls. These viruses require helper viruses such as herpes or adenovirus to replicate. These studies may provide insight into the immuno-pathogenesis in CFS.

Studies by Modra Murovska (Riga,Latvia) concluded that active infection with HHV6 and HHV7 is more frequent in CFS patients than in healthy blood donors. B19 DNA was also found in the plasma of patients but not controls. Reactivation of these viruses may lead to immune dysfunction.

Barbara Cameron (Sydney,Australia) presented further work from the Dubbo Infection Outcomes Study. This study looks at the evolution of CFS following PIFS prospectively. All 20 of the subjects (10 patients and 10 controls) were sero-positive for HHV6 and 10 were positive for CMV (5 patients and 5 controls) at baseline. Some EBV titres increased over time in patients and controls. Over time there was no correlation between symptom scores and antibody titres. The data do not support the hypothesis of ongoing active EBV,HHV6 or CMV in the pathogenesis of PIFS or CFS.

Session 5

Latest Research in Immunology

The immunological profile of an Australian CFS female population was presented by Ekua Brenu (Gold Coast,Australia). She noted a 0.2% prevalence of CFS is Australia, with $A59 million per annum spent in the management of CFS. Blood samples were taken from 8 CFS patients and 8 controls. Neutrophil function was studied with respect to respiratory burst and phagocytic activity. CFS patients demonstrated significant decrease in respiratory burst, but increased phagocytic activity did not attain significance. T cells, B cells and monocytes were observed in patients and controls.

Christopher Snell (Stockton,USA) did not find that either RNaseL ratio or elastase have any efficacy as biomarkers for CFS. There was high variability for both measures in CFS and controls, and these levels may be influenced by factors other than illness. RNaseL activity may not be unique to CFS.

Gordon Broderick (Edmonton, Canada) found that subjects with Gulf War Illness (GWI) can be discriminated by demonstrating significantly different neuro-endocrine-immune dynamics in response to exercise. Changes in cytokines, NPY and cortisol are evident both at rest and much more so under challenge, and could separate subjects completely from the control group.

Subgrouping of CFS patients was addressed by Vincent Lombardi (Reno,USA) looking at cytokine and chemokine profiles. He used microarray, a Random Forest computational programme, to delineate CFS patients from healthy controls. Each subgroup was found to display a unique cytokine/chemokine signature. This has potential to subgroup patients using serum biomarkers in an approach to appropriate treatments. (Anti-inflammatory, antiviral or antimicrobial).

Nancy Klimas (Miami,USA) has found that cytokine abnormalities are common in CFS, with potential as biomarkers or targets for treatment strategies. Cost effectiveness with newer techniques should make these tests more readily available to evaluate a large panel of cytokines. The study presented demonstrated a disorganized pattern of the cytokines regulating Th1 dependent lymphocyte function, critical to antiviral defence. The data supports a Th2 shift, proinflammatory cytokine cascade activation and down regulation of components of cytotoxic cell function.

Nicole Porter (Chicago,USA) showed the importance of looking at viral versus non-viral onset in CFS, with differences in cytokine production and expression. In the viral group there was Th1 shift and in the non-viral group a Th2 shift. Viral and bacterial onset patients should be separated in future studies. A pattern of protein production in the non-viral group is likely to be immune cell mediated anti-inflammatory activity with chronic suppression of immune system activation. In the viral group, there is pro-inflammatory activation with persistent hyper-immune response.

Session 6

Assessment Issues from Biological to Behavioural

Structural Equation Modeling (SEM) is a data-analytic technique. Brian Gurbaxani (Zurich,Switzerland) has used it to look at CFS heterogeneity. This is an attempt to integrate the variables in CFS particularly in relation to HPA and stress related variables.

Leighton Barnden (Adelaide, Australia) analyzed brain MRI images in 25 CFS subjects and 25 matching controls. Voxel

based analysis of the images was used, and a voxel was described as a 3D pixel. There were changes in the midbrain of patients, which could account for some of the CFS symptoms, such as changes in the reticular activating system and the red nucleus. No changes were seen in the amygdala and there was no significant difference in grey or white matter. Changes in the medulla and insular were consistent with the autonomic dysfunction seen in CFS.

A diagnostic test for the identification of metabolic dysfunction was discussed by J.Mark VanNess (Stockton,USA). Two graded exercise tests with cardio-pulmonary analysis were performed within 24 hours of each other. There was a “fatigue effect” of prior physical activity not characteristic of other illnesses. There was reduction of peak oxygen consumption and/or oxygen consumption at anaerobic threshold in CFS patients and in particular those with a high viral load. This provides evidence of metabolic dysfunction.

Norman Booth (Oxford,UK) described work on mitochondrial dysfunction in CFS. An “ATP profile test” has been designed for CFS and other energy depleted conditions. 5 factors were collated and multiplied together to produce the mitochondrial energy score. CFS affects every cell in the body and a mitochondrial disorder seems a likely possibility. This test is able to differentiate patients whose fatigue is due to psychological factors from those who have insufficient energy due to cellular respiration dysfunction.

Session 7

New Developments in Pediatric ME/CFS

Identification of biomarkers for CFS in children (8-17 years old) looking at specific genetic and innate immune parameters was the object of study presented by Ritchie Shoemaker (Maryland, USA). He had found an association of increased auto-immune abnormalities and elevated TGFβ, a cytokine associated with abnormalities in T regulatory lymphocyte function. All cases of CFS were clearly identified.

Leonard Jason (Chicago, USA) examined the criteria used to diagnose ME/CFS in pediatric samples. The 2006 criteria for diagnosing pediatric CFS evidenced 97% sensitivity and 100% specificity. Findings suggest that the 1994 Fukuda criteria are less effective in making a correct diagnosis, with only 76% sensitivity.

The clinical characteristics of 81 Belgian adolescents with Chronic Fatigue were described by Greta Moorkens (Antwerp, Belgium). One in three complained of headache or muscle ache, one in five complained about concentration or memory problems. Sleep studies and psychological testing was only performed in one in four of the group (probably due to parent or adolescent opposition) but were found to be abnormal in 60% of those tested.

Up to 68% of children with CFS are prevented from attending school, and the characteristics and recovery of these housebound children was addressed by Esther Crawley (Bristol, UK). Of 46 children assessed, 13 did not have a primary diagnosis of CFS, despite having been diagnosed by a pediatrician. This was a prospective study and at follow up (between 8 and 39 months) 4 had recovered completely and 6 were well enough to attend school. She then looked at whether patterns of symptoms suggest distinctive subtypes of pediatric CFS. She concluded that CFS is heterogeneous in children and the different factors may represent different underlying disease processes. Age, length of illness, anxiety or depression had no bearing on the 3 different factors identified by factor analysis. Cluster analysis identified 5 groups of children, which could be discriminated using regression analysis, which showed significant differences between the groups in terms of number of symptoms, fatigue and physical functioning.

Sanae Fukuda (Osaka, Japan) used sleep scores to distinguish between children at high risk of developing childhood CFS and general healthy students. The sensitivity of the sleep score was 85 with a specificity of 75.4. Intervention with sleep practices and CBT should be considered for high risk children. Also from Japan Kei Mizuno (Osaka,Japan) had looked at selective and divided attention in childhood CFS. Findings suggest that this maybe impaired. 3 types were identified. Functional MRI will be used to clarify the neural substrates associated with divided attention.

Session 8

Research Developments in Genetics

The session opened with an overview of Genomics in CFS by Jonathan Kerr (London, UK). 88 CFS associated genes have been identified by microarray. 85 are upregulated and 3 downregulated. Several other diseases have also been looked at. Clustering has identified 7 subtypes in the 55 patients studied, and 5 genes showed therapeutic potential. There is therapeutic potential in that 5 of these genes are known to be targeted by experimental or licensed drugs. These include some of the cancer and rheumatic drugs.

Microbial infections are associated with CFS, and it is hypothesised that specific organisms maybe associated with the subgroups. A trial of 62 patients (including 6 with Q fever) was undertaken. There were 14 with endogenous depression and 29 normal blood donor controls. Differential expression was seen for all 88 genes in the patient group. Similar genes were seen in the Q fever-CFS group. The depressed patients were similar to the normals except for 5 upregulated genes. QPCR datafor the 62 new patients were clustered with the 55 previously tested CFS patients. 8 subtypes were identified. 12 of the genes are known to be linked with the pathogenesis of EBV infection. Future work needs to look at larger cohorts, longer term studies and biological relevance of the subtypes.

Marc Fremont (Brussels,Belgium) reported on gene polymorphism, studies of which support the implication of intestinal dysfunction and activation of the Th17 axis in CFS. This opens a new perspective regarding treatment. The hypothesis that immune activation is mediated by Th17 cells in these patients is supported. There was a higher frequency of alleles making these patients more susceptible to gram negative enterobacteria.

Toni Whistler (Atlanta,USA) used gene arrays to look at the mediators of NK cell function. She found that there was decreased functional capacity of NK cells in Gulf War Illness. There was impaired immune function involving Th2 and proinflammatory cytokines, cytokines, cytotoxic NK cells and T cells, and dysregulated mediators of the stress response such as salivary cortisol. These differences were augmented by exercise challenge. Laboratory diagnostic tests maybe developed as a result of this research.

Further work from St George's,London was presented by Robert Petty (London,UK) who had looked at microRNA patterns in CFS. MiRNA expression was analysed in PBMC samples of 15 patients and 30 normals. Microarray analysis identified differential expression of 28 miRNA, 5 of which were confirmed using Taqman QPCR. Using this method, each of the 5 showed elevated expression in CFS with increases over 1.5 fold compared to controls. There is potential for this to be used as a biomarker.

Lihan Zhang (London, UK) discussed their gene database of 117 CFS patients. The 8 genomic subtypes had distinct differences in SF-36 scores, clinical phenotypes, severity and geographical distribution. Antibody testing was done for EBV, enterovirus, Chlamydia pneumoniae, Coxiella burnetii and parvovirus B19 an revealed subtype-specific relationships for EBV and enterovirus – both being common triggers in CFS. There is potential for treatment and further study is warranted.

A genome wide study of CFS identified candidate genes not considered in previous studies and was discussed by Mangalathu Rajeevan (Atlanta, USA). Polymorphisms were found to correlate with gene expression and were strong predictors of disease, and need further investigation.

Judy Mikovits (Reno, USA) concluded that preliminary data suggests that HLA and KIR variation might contribute to the risk of CFS. If HLA is not expressed, NK cells kill the target (viral infected) cells

Andrew Lloyd (Sydney, Australia) found that cytokine polymorphisms have a synergistic effect on the severity and duration of acute infective illnesses and PIFS. Analysis of samples from 300 patients who had had EBV, Q fever and Ross River Virus (from the Dubbo Infection Outcomes Study) were analysed. High producing IFNγ+874 T/A and low producing IL10-592C/A polymorphisms were both significantly associated with increasing illness severity. Variations in intensity of the inflammatory

response underpin the severity of acute illness and can predict the duration of PIFS across varied infections. He stressed the importance of looking at phenotypes prospectively. The Dubbo study found no evidence of persistent antigen or chronicity of cytokines.

Session 9

Advances in Brain Functioning

Elke van Hoof (Brussels, Belgium) discussed the issue that CFS influences cognitive functioning, attention and memory. There seems to be slower information processing. Her study examined reaction speed in CFS, and looked at whether this is negatively influenced by external stimuli such as physical complaints. It was found that CFS patients were more distracted by their bodily focus, which in turn negatively influenced cognitive performance. This slow processing speed is partially responsible for the cognitive malfunction in CFS. Tasks requiring complex processing are affected.

EEG data can discriminate 905 of CFS patients from healthy controls and patients with depression according to work by Frank Duffy (Boston, USA). The diagnostic label of CFS may often be misapplied in community practices, and this can lead to data discrepancies. This study has shown that CFS is a condition causing objective and measurable peturbations in CNS function.

Cognitive function in adolescents and young adults with CFS was presented by Laura Younis (Melbourne,Australia) The CFS patients did perform as well as controls on educational tests (verbal and mathematical) These findings were unexpected as the tests were challenging and fatiguing and involved a large neuropsychological test battery.. These patients had reported more school absenteeism, depression, sleep disturbance, cognitive dysfunction and other symptoms than controls. Strong motivation to perform well may not reflect typical performance of these students if they had been in an educational setting.

Assessment of amino acid neurotransmitter function was performed in CFS, major depression and healthy volunteers and was presented by Dikoma Shungu (New York, USA). There were no significant abnormalities in regional amino acid neurotransmitter function in CFS. There was confirmation of reductions in occipital GABA in major depressive disorder.

Session 10

The Japanese Experience

Yasuyoshi Watanabe (Osaka, Japan) gave a good overview of the Japanese development of anti-fatigue food and equipment. Animal and human studies were covered. They had developed scales for quantification of fatigue, and then tested a variety of products. Animal models were initially used to evaluate the effects of supplements, anti-oxidants and substances for energy. Many biological and physical measures were done. Various products were found to be of use. These included: 1).Applephenon – a polyphenol extract from unripe apples. 2) Imidazole dipeptide (high in chicken breast and animal muscle) which has an antioxidant effect and is produced as a drink. 3) Co-enzyme Q10. 4) Epigallo catechin gallate. 5) Crocetin (carotinoid dicarboxylic acid) from the crocus flower. Physical therapies found to be of use included mildstream bathing (a micro-bubble bath). Animal therapy and music therapy were among other approaches found to be of use.

The relationship between fatigue and diet was covered by Hirohiko Kuratsune (Osaka, Japan). A 20 item questionnaire was administered to 131 female students, and they were then classified according to the fatigue score. It was found that students frequently missed breakfast and lunch. There was low calorie, fat and carbohydrate intake in the most fatigued. Very significant fatigue correlated with low rice, fish and omega 3 intake. Zinc, copper and magnesium, vitamins B6 and B12 were all low in the severely fatigued. Autonomic nervous system activity using HRV analysis was also studied in fatigued patients. A relative sympathetic nerve dominance was associated with the fatigue state.

Chaos analysis was used to evaluate the fatigue state associated with labour, and discussed by Seiki Tajima (Osaka, Japan). Overwork is a big issue in Japan. Beverage factory workers were assessed using the Artett C system. Subjects

were divided into 3 groups depending on fatigue level, and autonomic function was assessed. There was no significant difference in the 3 groups using analysis of maximum lyapunov exponent and correlation dimension analysis, and between low frequency and high frequency ratio (spectral analysis). This is the ratio between the sympathetic/parasympathetic systems. Further studies are needed to reveal differences from pathological and recoverable fatigue using these methods.

The pathophysiology of CFS in childhood in Japan was presented by Teruhisa Miike (Kobe, Japan). Japanese children are found to be often active till late at night, exposed to a lot of bright lighting and a hard daily schedule coupled with excessive information from TV, games, cell phones etc. Despite going to bed very late, children still need to get up early, and thus become sleep deprived. There is a breakdown in the body clock. They can then suddenly develop a hypersomnia type sleep disorder and childhood CFS. Long sleep gives no improvement, and many symptoms occur fitting the criteria for CFS. Activated enzyme depletion leads to mitochondrial dysfunction. There is decreased cerebral blood flow. There may also be increased risk of cancer. The aim should be to prevent this set of circumstances.

POSTER PRESENTATIONS

A large number of posters were presented with a wide range of topics from around the world. I was not able to view them all, but those I did manage to see are described:

Pharmacologic and non-pharmacologic treatment advances

Effectiveness of oral NADH in the treatment of CFS - Jose Allegre (Barcelona Spain) concluded that oral NADH does not seem to modify clinical variables, but some benefits were seen in anxiety levels, but depression increased. In effort tests there was some significant reduction of maximum FC.

Partner relationship influence on functional capacity in CFS women – A.Blazquez (Barcelona,Spain) – Neurocognitive dysfunction correlated positively with the relationship and significantly influenced ventilation and supramaximal exercise.

Role of erythrocyte aggregation and deformability in CFS – Ekua Brenu (Gold Coast<Australia) – found that there were no abnormal changes in the rheological characteristics of erythrocytes in CFS. Deformability and aggregation are not therefore likely to be markers for CFS.

Post-Cancer Fatigue (PCF) is not associated with altered cytokine production – Barbara Cameron (Sydney,Australia) – findings argue strongly against the notion that PCF is mediated by peripheral inflammation.

Pacing as a dynamic embedded, embodied treatment/prevention strategy in CFS – Bruce Carruthers (Vancouver,Canada) – Pacing is a strategy that patients learn gradually to adjust their activity/rest sequences and treat their fatigue in a preventative way.

Oxygen toxicity as a locus of control for CFS – Paul Cheney (Ashville, USA) – Concluded that CFS is an oxygen toxic state. This is less a cause of CFS but a final common pathway downstream from etiologies, but which may determine outcome.

Cell associated therapy for CFS – Paul Cheney (Ashville,USA) – has found that therapy with low molecular weight peptides from cell-associated mammalian tissue homogenates (porcine) appear to offer significant benefit in CFS. Use of several tissue extracts appears to be more successful than only one.

Oxymatrine for the treatment of CFS associated with chronic enterovirus infection – J.Chia (Lomita,USA) – This treatment showed significant benefit, with a shift in immune response in the Th1 direction, which correlated with symptomatic response. Oxymatrine maybe an effective immune modulator in CFS before definitive antiviral therapy becomes available.

Serving Students with CFS and other chronic illnesses – Patricia Fennell (New York, USA) – described a workshop for educators to discuss the needs of of those with chronic illnesses. As a result educational services can be improved for

students using the Fennell Four Phase Model.

US Government strategy and funding of CFS research compared to similar illnesses – Kenneth Friedman (Newark, USA) – Of the US Government research effort into neuro-endocrine-immune disorders (NEIDs), Lyme disease has shown the most progress. Despite the government spending more on GWI there is still no diagnostic test or specific medication. New research strategies and funding mechanisms are needed for illnesses such as CFS.

Amygdala retraining techniques may improve outcomes for patients with CFS – Ashok Gupta (London,UK) – had done a clinical audit of subjective outcomes. This revealed higher rates of improvement in comparison to remission rates in other intervention studies. No control or placebo group was used and future studies will incorporate this.

Treatment of Cryptostrongylus pulmoni, a new parasite found in CFS – Lawrence Klapow (Santa Rosa,USA) – This is a chronic roundworm parasite found in a number of patients studied. It reproduces in the lungs and GI tract. It appears to trigger CFS symptoms during its reproductive stage. Symptoms were relieved with Ivermectin, weekly inhalations with nebulised ethanol and treatment of the GI tract with anthelminthics.

Predictors of fatigue in patients with MS – Anners Lerdal (Drammen,Norway) – The main predictors of fatigue were fatigue scores and fatigue caseness at baseline. Poor general health and perceived cognitive impairment also predicted higher levels of fatigue.

Is there an association between exposure to chemicals and CFS? – Luis Nacul (London,UK) – existing evidence remains inconclusive as to the association between exposure to chemicals and CFS, and there is need for well designed epidemiological studies.

Similarities of CFS and autism spectrum disorders: comparison of blood co-infections – Garth Nicolson (Huntingdon Beach,USA) – Chronic infections are similar in both those with CFS and a large subset of patients with neurobehavioural disease. The 3 infections seen were mycoplasma species, Chlamydia pneumoniae and HHV6.

Effects of a dietary weight supplement on fatigue, appetite suppression and weight-loss: implications in CFS – Garth Nicholson (Huntingdon Beach,USA) – The product used was an amaylase inhibitor plus NT factor (HealthyCurb). Notable appetite suppression occurred coupled with significant weight loss. The group showed an overall decrease in fatigue, with improvement in lipid profiles and cardiovascular health. There were no adverse effects clinically or biochemically. This seems a safe option for those with CFS wanting to lose weight.

Improved renal function in CFS patients with IV immunoglobulin treatment – Tae Park (Seoul,Korea) – Improved renal blood flow as a result of this trial may be evidence of corresponding cerebral blood flow, as patients on treatment experienced improved cognition. A further poster looked at the risk of CFS patients developing chronic kidney disease. The risks showed decreased glomerular filtration rate in many CFS patients, and recommendations are that kidney function should be checked regularly in CFS. Cognitive function was further investigated in another poster with positive outcome in those treated with IV immunoglobulin.

Lymphatic drainage of the neuroaxis and the central rhythm impulse – Ray Perrin (Preston,UK) – hypothesized a model for pathological links to CFS. Cranial rhythm impulse may be the rhythm produced by a combination of cerebrospinal drainage of the neuroaxis and sympathetic induced pulsations of the central lymphatic drainage. Osteopathic manual treatment can reduce the severity of CFS.

Muscle fatigue in CFS and its response to a novel manual therapeutic response – Ray Perrin (Preston,UK) found that post-exercise muscle function in CFS is improved following specialized osteopathic intervention. Fatigue in this disorder is considered not due to myopathic changes, but a consequence of other extrinsic causes, such as a reduction in lymphatic drainage.

VDR receptor competence induces recovery from CFS – Amy Proal (New York,USA) – has a working model of CFS in which a micorobiota of chronic pathogens accumulate a metagenome that is able to dysregulate the innate immune response, and cause the systemic inflammation characteristic of the disease. The process has been reversed using a VDR agonist (olmesartan medoxomil) and sub-inhibitory antibiotics.

A parent advocacy guide advising how to obtain educational services for children with neuroimmune disease – Laura Baker (Santa Barbara,USA) and Karla Rogers (Nevada City,USA) produced a comprehensive resource guide to assist parents meet their child's educational needs.

Utilization of CFS continuing medical education courses – Hao Tian (Atlanta,USA) – this course was described and confirmed as an important online source for continuing medical education. There is a well utilized Primary Care course and one for allied health professionals. In a 5 month period, 283 participants received CME certificates.

The self-regulatory model in women with CFS and MS: illness representations, coping strategies and outcome - Elke van Hoof (Brussels,Belgium) – Patients were shown to determine the degree of dysfunction and illness related behaviours in relation to their subjective experience of the disease. Findings in the study will help determine what strategies may be effective in improving function.

Treatment study of methylation cycle support – Richard van Konynenburg (Springfield, USA) – Treatment designed to support the methylation cycle appears very promising and seems worthy of a more controlled study. Results are consistent with the glutathione depletion-methylation cycle block hypothesis for CFS. Treatment included hydroxocobalamin, 5-methyltetrahydrofolate and folinic acid, with nutritional support.

Virology/microbiology Research

Post-infectious fatigue syndrome following giardia infection – an ongoing multidisciplinary five-year follow-headed by Prof Harald Nyland – presented by Eva Stormorken – (Vaaler, Norway) – Findings support the existence of PIFS following giardiasis. Interventions consisted of medical care, clinical assessment and an educational course. Currently a work-related rehabilitation programme is taking place. Prospective studies are required to determine functional outcome.

6 years experience in a specialized unit in the diagnosis of CFS – José Alegre (Barcelona,Spain) – The SFC is the main tool for diagnosis in this specialized unit. A variety of diagnoses of fatigue are described. Analytical, imaging and psychiatric assessment did not provide diagnostic tools adequately.

Family response when a parent has CFS – Julie Donalek (Chicago,USA) – A wide range of effects on the family are presented such as "a changed life", "a shrinking exterior world", reorganizing family management", "struggle for normalcy" etc These issues need to be addressed for the family as well as the patient.

Socio-demographic variables, depression, sleep quality and functioning, and the relationship to fatigue in the acute phase of a stroke - Anners Lerdal (Oslo,Norway) – Symptoms of depression and poor general health are related to the experience of fatigue in these patients, suggesting the need for further research into the complex nature of fatigue.

Prevention of CFS – Phillipe Tournesac (Dijon,France) – A questionnaire has been developed to identify patients described as "hypersensitive" and more likely to develop illnesses such as CFS and FM. This could provide a means of identification and preventing the evolution of toward CFS and related syndromes. Many simple preventative approaches can be included such as sleep, nutrition and exercise.

Could CFS be caused by allergen-induced immune activation in individuals who respond with excessive and prolonged cytokine production due to variant genes, and who have enhanced susceptibility to cytokines. – Gina Watkins (Sydney,Australia). A literature search was presented together with further study from the Dubbo infection outcomes. This confirmed that further research is needed looking at the immune response and cognitive function following allergen exposure.

Remodeling of lymphocyte-cytokine networks in GWI under challenge – Gordon Broderick (Edmonton,Canada) – Characteristic immune responses occur spontaneously in these patients after exercise challenge, and resolve once the challenge is removed. Results suggest a potential shift in the regulation of body fat and energy metabolism in GWI and a bias toward Th2 mediated humoral immune response.

A comprehensive analysis of serum cytokines in PIFS: a masked case control study – Barbara Cameron (Sydney,Australia) – The data did not support the hypothesis of ongoing cytokine activity in the circulation in the pathogenesis of CFS or PIFS.

Comparison of immunoperoxidase staining of stomach biopsy, neutralizing enterovirus antibody and whole blood viral RNA testing, for the diagnosis of chronic enterovirus infection in patients with CFS – John Chia (Lomita,USA) – EV VP1 staining of stomach biopsy is more sensitive than either commercially available neutralizing antibody test or qualitative enteroviral RNA determination of the blood, for the diagnosis of chronic enteroviral infection. Elevated EV antibody titre can confirm the particular serotype involved.

Decreased perforin and granzyme protein expression of cytotoxic T cells and NK cells from CFS patients – Deborah Goetz (Reno,Nevada) – this study corroborated the Klimas et al study. NK cells showed altered expression of PRF1 and GZMB not due to increase in CD56 subset. T cell abnormalities suggest prior antigen exposure and possible impaired memory function.

A re-analysis of the Dubbo Infections Outcomes Study post infective fatigue cytokine dataset. – Brian Gurbaxani (Sydney,Australia) – Cultured cytokine values do appear to oscillate over time. The oscillations may help distinguish PIFS cases from controls within each infective group, and appear to be different for each of the 3 infections studied. (EBV,Ross River Virus and Q fever)

Ion channel function and CFS – Susan Hagan (Glasgow,UK) – Identification of changes in gene expression of a number of ATPase enzymes and ion channels using DNA microarray indicates a potential role for ion channels and ATPase function in the pathology of CFS. This may help formulate a rational hypothesis for the pathogenesis of CFS.

The RNAseL antiviral pathway and its role in chronic inflammation and CFS – Vincent Lombardi (Reno,USA) – Results confirm that proteosymal degradation of RNaseL is triggered by PMA in human cell lines, and this inflammatory response can be prevented by anti-inflammatory agents that block NF-κβ.

TGFβ-1 in the treatment of autoimmunity in CFS associated with HLA DR by PCR – Ritchie Shoemaker (Pocomoke,USA) – The ability of losartan (up to 50mg daily), an angiotensin receptor blocker, labeled for treatment of hypertension, to lower TGFβ may affect TH17 cells that in turn affect T regulatory cells. Losartan may have a role in the innate immune abnormalities in CFS.

Assessment issues from Biological to Behavioural

Measuring fatigue pre and post exercise using SF-36, MFI-20 health and wellbeing surveys – Katie Baroni (Stockton,USA) – the SF-36 and MFI-20 clearly differentiate between CFS and controls. The SF-36 did not detect significant pre to post test changes in the CFS group.

Functional impairment in an environmental clinic sample – Alison Bested (Toronto,Canada) – a wide representation of the profiles of 128 CFS patients diagnosed with CFS,FM and MCS. Results were consistent with findings in other countries and patients' reported difficulties working and caring for homes and families. Early comprehensive assessment and medical management, social support, and assisted non-discriminatory access to consistent financial means could avoid deterioration associated with prolonged illness.

Diagnosis of CFS – Bruce Carruthers (Vancouver,Canada) – describes clinical experience with comments regarding the influence of different attitudes on the process of diagnosis of CFS and other syndromes. 3 issues are covered: nominalist attitude, complementary attitude and causal influences felt directly in everyday life. He comments that we do need to pay

more attention to the earlier phases of diagnosis not just the end point.

Unusual dietary intake among CFS patients – Alexandra Caspero (Stockton,USA) – a diet history questionnaire (NIH) was used. Dietary interventions maybe efficacious as adjunct therapy.

The emergence of fatigue science – Fred `Friedberg (New York,USA) – A study of literature on pain and fatigue were reviewed. The study provides encouraging signs of increased scientific attention to fatigue. The future direction of fatigue research is uncertain as there is no clearly delineated domain of fatigue with respect to both peer review journals and federal funding.

Replication of an empirical approach to delineate heterogeneity of CFS – Brian Gurbaxani (Sydney,Australia) – Data support the contention that chronic medically unexplained fatigue is heterogenous and can be delineated into discrete endophentypes, and this should be pursued further. This could help understand etiology and provide more patient focused treatments.

Frequency and content analysis of CFS in medical textbooks – Leonard Jason (Chicago,USA) – Findings suggest that CFS is underreported in medical textbooks. There is a need for CFS to be more represented in text books, with more comprehensive coverage provided to include etiology, prevalence, criteria and treatment options.

A closer examination of cardio-pulmonary test-retest effects in CFS – Kylie Kumasak (Stockton,USA) – Reductions in VO2 max were similar to previous studies, The reductions seen in VO2 max on test-retest were not due to differences in maximal effort. Future test should include prescreening criteria of post exertional malaise to increase the likelihood of observing metabolic abnormalities in CFS.

Prevalence and risk factors for CFS in women in S Brazil – Luis Nacul (London,UK) – CFS and probable CFS are not uncommon in the study. Different factors were identified in these 2 groups, and the importance of using specific diagnostic criteria and subgrouping of cases in research and clinical practice was emphasized.

Trends in knowledge about CFS by Brazilian doctors – Luis Nacul (London,UK) – the ability of doctors in Brazil to diagnose this illness remains poor, but there is a trend towards a move from psychological to medical interpretations of a typical patient with CFS. Education of health professionals and the population about CFS is thus warranted.

Trends and predictive value of CFS diagnosis labels given by GPs in England – Luis Nacul (London,UK) – Diagnostic labels vary in time and across GP practices. This needs to be taken into account when estimating prevalence of CFS in primary care.

A survey of the health needs and experiences of people with CFS in a NHS specialist service in England – Sue Pemberton (Leeds,UK) – These patients have varied needs, necessitating the importance of a multidisciplinary team. The interpersonal skills and engagement with the patient are as important as the intervention itself. A model is being developed to guide professionals dealing with this illness.

An audit of the clinical outcomes of a multi-disciplinary service for CFS – Sue Pemberton (Leeds,UK) – Minimum data set was used in this audit done at one year from entry into the service. There was a positive overall effect, particularly in symptom related outcomes. Functional outcomes did not show significant change, but this may be due to patients being asked to balance out activity levels initially.

WORKSHOPS

Before the formal conference 4 workshops were available and well attended:

WORKSHOP 1

Treating pain, sleep and fatigue – Charles Lapp and Lucinda Bateman

This presentation was divided into the 3 parts and gave an excellent overview of the 3 topics and included case studies. Much discussion was generated.

PAIN

Treatment of pain was addressed non-pharmacologically and pharmacologically.

Non pharmacological approaches included:

Pacing

CBT

Counselling, hypnotherapy, biofeedback

- Restora tion of sleep
- Gentle physical conditioning (stretching, strength, aerobic)
- Massage therapy, physical therapy etc.

Pharmacological tools included:

- Anticonvulsants: Pregabalin, gabapentin, topiramate, zonisamide
- Serotonin norepinephrine reuptake inhibitors: Duloxetine, milnacipran, venlafaxine
- Dopamine agonists under study: pramipexole, ropinirole,
- Hypnotics under study: sodium oxybate
- Opiods: (a last option) – less effective for chronic than acute pain, severe side effects, withdrawal problems. Tramadol, methadone, hydrocodone, oxycodone, morphine, fentanyl,subooxone

SLEEP

No specific sleep disorder is characteristic of defining CFS/ME/FM, but sleep disorders are highly prevalent. Management of sleep seems to be the key to improvement.

Characteristic sleep patterns:

- Non-restorative sleep
- Difficulty in initiating and maintaining sleep
- RLS/PLMS
- Nocturnal myoclonus
- Vivid dreams/nightmares
- “Tired but wired”
- Phase shifting
- Dysania

Undiagnosed sleep disorders should be considered. Upper airways resistence disorder (UARS), when patients do not meet criteria for obstructive sleep disorder is common in CFS. This is accompanied by eratic breathing, drop of oxygenation, frequent arousals and daytime fatigue plus other symptoms. Treatment may relieve some symptoms.

Treatment of sleep disorders associated with CFS

- Rule out sleep disorders
- Sleep hygiene
- CBT
- Medication:
- Reduction of pain (as above)
- Dopamine agonists: ropirinole, pramipexole (RLS,PLMS)
- Simple measures: antihistamines, melatonin (watch for rage reactions at high dose)
- Non-benzodiaepines: zolpidem, eszopiclone, zaleplon, ramelteon
- Clonazepam: (myoclonus, restlessness)
- Tizanidine: may enhance sleep and reduce self talk
- Tricyclics: amitriptyline, cyclobenzaprine

Sleep maybe disturbed by benzodiazepines, some opiates, some SSRIs and DOPAs,Alcohol

FATIGUE

This session covered general causes of fatigue, and there seems no way to really define or measure it. There are many different types of fatigue reported. Fatigue may be physical, mental/cognitive or motivational. The nature and severity of fatigue must be addressed, and this incudes: Interference with daily activities, post-exertional effects, diurnal effects and relief or not by rest. Mood disorders have a complex association with fatigue.

A number of fatigue measuring instruments were evaluated.

Management of Fatigue:

- Elimination of sedating medication
- Treatment of depression
- Structured schedule
- Activity/exercise plan
- Stimulants: caffeine, amantidine, methylphenindate, modafinil
- Antidepressants: Bupropion, fluoxetine
- CBT
- Self care techniques: books, CDs etc, coping skills, Campbell course
- Gupta course
- Emotional support
- Cognitive techniques (distraction, prioritization, reframing)

WORKSHOP 2

Behavioural assessment and treatment of ME/CFS – Fred Friedberg and Leonard Jason

This workshop focused on the understanding of ME/CFS and the management from a behavioural point of view. Leonard Jason began with a good overview of the history, biological, social and psychological factors in this illness, the importance of accurate diagnosis and how to distinguish the illness from anxiety and depression. This was followed by a presentation covering the behavioural assessment and treatment of CFS by Fred Friedberg. Sleep management, pacing, behavioural intervention, coping skills and the importance of emphasizing pleasurable feelings were all covered in depth.

This was a session in which audience participation and much interaction was involved. There was a wide range of participants from disciplines of general medicine, psychiatry, reseach, psychology and complementary medicine. Questions and areas of interest were posed by the audience, which were then ably covered by the 2 leaders, with their background of wide experience, expertise and research work. Many different techniques were discussed among the audience looking at

CBT, simple strategies to improve coping skills, the importance of social support and relaxation approaches.

By the end of the workshop, after much interactive discussion, most people came away feeling there were plenty of simple options to offer patients with this perplexing illness.

I was not able to attend the following 2 other workshops, as one had to make a choice, and I hope these will be covered by another attendee.

WORKSHOP 3

How to apply for grants – Eleanor Hanna.

This was an informal workshop with Dr. Hanna on a speaker phone from NIH, as she was unable to attend in person.

Nancy Klimas, Lenny Jason, Mary Ann Fletcher, and Fred Friedberg, all experienced grantees, also answered questions about applying for grants. Dr. Hanna, our CFS contact person at NIH, fielded questions about the NIH application process. A networking lunch for about a dozen interested workshop participants was arranged and well-attended.

WORKSHOP 4

Research 101 – Suzanne Vernon

This workshop presented research approaches for how genomics could inform clinical practice of CFS. Suzanne Vernon first provided evidence that chronic diseases are some of the most common maladies of the 21st century and how genomic approaches could improve diagnosis, treatment and ultimately prevent chronic diseases. We discussed how CFS puts the aspirations of genomic medicine to the test since CFS is a complex phenotype controlled by many genes and whose inheritance does not follow the simple rules of Mendelian genetics. This means that genes and gene products are context dependent and in the case of CFS, potentially affected over time by other diseases and comorbidities, infection, trauma, and behavior.

We than discussed how high-throughput genomics will influence medical practice. With new biology and technology, we now can identify gene-environment causes of CFS, we can develop early detection methods and we can determine of molecular basis CFS taxonomy. Genomic profiling has been used to identify “subtypes” of CFS that are related to both pathophysiology and etiology. There are examples of several examples of using genomics to customize therapeutic interventions in a variety of diseases and there is recent evidence to support this approach for CFS.

The greatest opportunity to inform medical practice as it relates to CFS will come from applying new technologic and computational tools to well designed human observational and clinical studies that include collection of rich and relevant data. Suzanne emphasized the need for good study design and stressed that new technology should be used to identify early detection markers as well as diagnostic and subtype and treatment markers for CFS. We discussed a genomic medicine model for CFS and how adaptation of this model will influence not only the diagnosis and treatment of CFS, but will allow for the design of smaller, focused clinical trials and the tailoring of treatment to the biological profile of the patient and CFS.

Suzanne provided all participants with a USB drive that had a copy of her presentation as well as a file on personalized medicine. The session lasted for 3 hours and seemed to hold the interest and attention of the participants.

ROSAMUND VALLINGS, MB BS

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