

AACFS 7th International Conference summary

The 7th American Association for Chronic Fatigue Syndrome (AACFS) international conference was held in October. This annual conference brings together clinicians, researchers, patients and activists from around the world. ANZMES' Dr. Rosamund Vallings MB BS attended and in this article she gives us a summary of what was presented.



This conference was held in Madison, Wisconsin from 8 – 10th October, 2004. A day of research presentations was followed by two clinical days with a patient conference running alongside. I felt privileged to attend the research and clinical segments.



RESEARCH CONFERENCE

RESEARCH OVERVIEW, by A.Komaroff (Boston).

In Chronic Fatigue Syndrome, functional status is much reduced in all areas and \$9 billion is lost annually in productivity in the USA. Over time 10% of sufferers can expect complete remission and 23% will receive an alternative diagnosis eventually. The illness follows a relapsing and remitting course, and research has shown abnormalities in many systems:

Brain:

- Abnormalities seen on MRI and SPECT scans
- Cognition – IQ within normal range, but marked difficulties in mental processing etc.
- Sleep – polysomnographic abnormalities, with up to 28% increase in non-refreshing sleep.
- Neuro-endocrine dysfunction
- Autonomic dysfunction – basal and postural hypotension, reduced peak O₂ consumption and haemodynamic instability

Immune activation:

Activated lymphocytes cross the blood-brain barrier leading to microglial activation and perivascular activation. These effects can last decades, and lead to the secretion of pro-inflammatory cytokines and nitric oxide, with resulting injury to the peripheral nervous system and chronic low level immune activation in the brain. There is also increased neutrophil apoptosis.

Microbiological studies:

Many different post-viral fatigue states have been described. Examples include:

- Enteroviruses (Coxsackie, polio, echo) – abnormal lactate response to sub-anaerobic exercise

demonstrated. Enteroviral RNA in muscle without γP-1 protein suggests defective viral replication.

- Q Fever (rickettsial) – nucleic acid persists for up to 10 years in circulating mononuclear cells.
- Parvovirus: ongoing elevation of IFN γ with associated fatigue.
- Mycoplasma: found in up to 68% of European CFS patients (5.6% in controls)

Energy metabolism

Disturbances seen in urinary metabolites: such as depletion of amino-hydroxy-N-methyl pyrrolidine, slight elevation of β alanine and depletion of UM2 (serine).

Gene expression:

The genes involved in immune activation and energy metabolism are turned on more often in CFS.

Vitamin D connection:

Low levels lead to musculo-skeletal pain. Patients who have fibromyalgia tend to have lower plasma levels of Vit D as do people living in areas with long periods of darkness in the winter, with resultant tendency to osteoporosis.

Treatment:

Placebo controlled trials of treatment with omega-3 fatty acids have shown benefit in CFS. There is decreased production of inflammatory mediators and direct antiviral activity. Endogenous levels may be reduced by chronic viral infection.

EPIDEMIOLOGY OVERVIEW, by W C Reeves (Atlanta)

Fatigue is a very common symptom in medical practice, involved in up to 50% consultations of which 75% are psychiatric. The prevalence of CFS (existing cases) in the US is 4 - 75 per 100,000. Onset is usually sudden and average duration is 5 years (range 2-7 years). In the US it is more common in rural areas, with a pre-dominance in females and lower socio-economic groups. Minority races are at greatest risk. Annual loss in productivity in the US is \$US9 billion and the average annual loss in family income due to CFS is \$20,000. In the UK,

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\$US4 billion is spent on direct costs such as medication. Patients are often as severely or more disabled than those with heart failure or COPD.

FIBROMYALGIA OVERVIEW, by D Clauw (Michigan)

There has been a paradigm shift in diagnosis of fibromyalgia (FM) considering tenderness as part of a continuum rather than relying on definite numbers of specific tender points. The tenderness is usually diffuse, and using tender points for diagnostic purposes is affected by anxiety, expectation and distress. Random measures of tenderness are more relevant and accurate.

Causes of FM include a strong genetic tendency, and abnormality in pain-processing. This correlates with abnormalities in other sensory areas such as light and sound. There is generalised hyperalgesia and allodynia. Pain processing is either psychological (expectancy, hypervigilance) or neurobiological (peripheral or central). Dimensions of pain may be sensory, cognitive or affective.

Functional MRI (fMRI) shows brain changes correlating with pain experiences and there is no correlation with depression. Cognitive factors such as catastrophizing and loss of locus of control may cause changes in pain processing and correlate with poor prognosis. Other regional pain syndromes show similar changes in fMRI to that seen in FM.

Treatment: SSRIs, tricyclics and norepinephrine reuptake inhibitors all have some benefits in FM. Amitriptyline and imipramine are more analgesic than nortriptyline. Milnacipran is a new drug showing promise.

MICROBIOLOGY and IMMUNOLOGY

This part of the conference was introduced by Dharan Abalashi who listed the many viruses and other microbial agents studied in relation to CFS. HHV6, enteroviruses, Mycoplasma, Chlamydia and parasitic infections are all creating interest.



R.Suhadolnik (Philadelphia) discussed the current immunological situation, 20 years after the Lake Tahoe epidemic, and reported on a recent study of 66 CFS patients, 62 controls and 51 depressed patients. CFS patients showed marked impairment compared to the other two groups. The study supports the cytokine/immune activation model, showing direct correlation between the abnormalities in the RNaseL pathway and NK cell function. The 37/80 kDa ratio strongly correlated with the changes seen in CFS and symptom severity. The RNaseL activity leads to an ion channelopathy with patients experiencing many symptoms.

C.Raison (Atlanta GA) had experience with the use of IFN α in the treatment of Hepatitis C. IFN (interferon) is a cytokine released early in viral infection and causes a variety of symptoms including fatigue. 109 patients receiving IFN α -26 for treatment of hepatitis C were studied. During treatment 70% of patients reported marked fatigue and 30% developed symptoms sufficient to fit the criteria for CFS. ($p=0.0001$) This study supports the role of antiviral immune response in the pathophysiology of fatiguing illnesses.

J.Jones (Atlanta GA) reviewed the Dubbo Infections Outcome Study on behalf of Sydney colleagues. Patients who had had infectious mono, Q Fever and Ross River virus were followed up. He concluded that post-infective fatigue states (PIFS) following documented infection represent a valid and informative model for CFS. CFS occurred in 10% after these illnesses. Severity of the primary illness was the strongest predictor of development of PIFS and was not associated with premorbid psychiatric characteristics.

Signal transducers and activators of transcription (STAT) are a family of proteins playing a central role in the responses of cells to cytokines and were discussed by K.Knox (Milwaukee WI). She suggested that a study of a sub group of CFS patients who had an abnormally low STAT1 response to interferons, may explain the increased susceptibility to infections sometimes seen in this illness.

Decreased NK cells cytotoxicity is a frequently reported abnormality in CFS patients, and K.J.Maher (Miami FL) reported abnormalities in cytotoxic T cells and NK cells including reduced perforin and reduced concentrations of Granzyme A and B. These changes may provide biomarkers in the future.

D.Raciatti (Chieti, Italy) reported on a study of 130 patients looking at the potential role of STDs in the pathogenesis of rheumatological syndromes characterised by prolonged fatigue. Significantly high percentages of infections with Chlamydia, Ureaplasma and Mycoplasma were found serologically and when treated there was recovery from fatigue and other symptoms.

M.Fremont (Brussels, Belgium) discussed immune dysregulation associated with interferon α synthesis. He explained how RNaseL is cleaved by apoptotic and inflammatory proteases, and said that Mycoplasma infections are strongly associated with RNaseL cleavage. PKR is also shown to be activated in the PMBCs of CFS patients, and this can lead to immune dysregulation and induction of iNOS, with resulting muscle dysfunction and CNS and neuro-endocrine dysfunction such as hypothyroidism with intense fatigue

EPIDEMIOLOGY

D.Wagner (Atlanta GA) compared two scales measuring fatigue and health; the MFI and the SF36. These two scales as anticipated were found to be negatively correlated i.e higher fatigue associated with lower mental functioning, and this supports the construct validity of the MFI.

Artificial neural networks are computer generated networks likened to the human brain and are used for example, to help with decision making. A system has been devised, and was described by A Morris (Chicago) to help determine the types of symptoms that maybe useful in diagnosing CFS. Two different networks were created with 26 relevant questions common to both networks, but this is early stage work and cannot yet be generalised.

H.Harrison (Phoenix AZ) produced support for the hypothesis that there are genetic contributions to coagulation protein abnormalities seen in some CFS/FM patients. Distinguishing these factors may help to guide therapy.

R Underhill (New Jersey) in a pilot study showed that secondary cases of CFS occurring in unrelated household members may indicate that a low level infectious agent causing CFS may persist and be shed into the environment. Increased prevalence in genetic relatives indicates that genetic factors maybe involved in a subgroup of CFS patients.

NEUROPHYSIOLOGY

J.Stewart (New York NY) overviewed the varieties of orthostatic intolerance in CFS. He described three types of peripheral blood flow in these patients: low flow, normal flow and high flow. During orthostasis it was shown that there is enhanced thoracic hypovolemia related to inadequate cardiac venous return.

H.Kuratsune (Osaka, Japan) showed results of PET scans showing cerebral hypoperfusion in CFS suggesting that CNS dysfunction maybe related to the neuropsychiatric symptoms found in CFS. Density of 5HTT in the anterior cingulate cortex was significantly reduced in a study of CFS patients and this was negatively correlated with pain scores. This alteration in serotonergic neurons is thought to play a key role in the pathophysiology of CFS. These results may help explain why SSRIs are sometimes helpful in CFS patients.

Elastase activity in relation to impaired exercise capacity in CFS was demonstrated in a study presented by J Nils (Brussels, Belgium). The data provides evidence for an association between intracellular immune dysregulation and impairments in cardiorespiratory fitness. Results

showed correlation between increased elastase activity and exercise functionability and maybe related to impairments of lung diffusion and oxygen delivery to the tissues. NB Antibiotics decrease elastase activity in humans.

Reduced cerebral blood flow (CBF) in CFS was further confirmed in a study presented by K.Yoshiuchi (Newark NJ), who also found that psychiatric status and severity of illness do not play a role. Xenon CT was used which provides absolute measures of CBF.

PHYSIOLOGY

S.Levine (Columbia) analysed the metabolic features of CFS using multislice 1H MRSI. There was elevated lactate production in a significant number suggesting the possibility of a mitochondrial metabolism dysfunction. Elevation of thalamic choline was also demonstrated in some patients, suggesting the presence of neuronal damage.

U.Hannestad (Stockholm, Sweden) showed in a small study that the more severe the symptoms of CFS the greater the excretion of β -alanine. The level in one patient was exceedingly high and was associated with severe symptoms. There are structural similarities between β -alanine and GABA, and high concentrations in the CNS may account for some of the typical CFS symptoms. Symptoms similar to CFS are often seen as side effects in those with epilepsy being treated with drugs which increase GABA.

M.Fremont (Brussels, Belgium) presented a further study showing that cells expressing ankyrin fragments of RNaseL have been demonstrated, and this can contribute to increased sensitivity of patients to chemicals including heavy metals. Involvement in the maintenance of Th1/Th2 balance by interaction of the multidrug-resistance protein (MRP-1) and the ankyrin fragments is also relevant in CFS.

M.Pall (Washington State) described a number of mechanisms operational in CFS and related illnesses and produced evidence of increased nitric oxide and peroxynitrite levels in CFS, which lead to oxidative damage and further increase in cytokine levels. He described Vitamin B12 as a nitric oxide scavenger, which may help explain why some people do well on B12 despite having normal blood levels.

CLINICAL CONFERENCE



The day began with an excellent overview of the previous day's research papers by A Komaroff. Presentation of clinical papers then followed.

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A.Lyden (Michigan MI) presented evidence that two disparate sensory experiences (somatic pain and exertion during exercise) are processed similarly in patients and controls. There is a left shift in FM patients, who feel more pain at the same time as feeling more "work".

CFS patients were shown by C Javierre (Barcelona, Spain) to have lowered oxygen uptake when exercising. She had compared CFS patients with sedentary and physically active people using both an exercycle and an arm ergometer. Maximum power output was higher for all groups on the cycle as compared to the arm ergometer.

J.Alegre (Barcelona,Spain) evaluated 511 outpatients at a fatigue clinic and found that 350 fulfilled the CDC criteria for CFS. These patients had substantial reduction in physical and work activities. 50% experienced gradual onset and there was significant elevation of RNaseL. 10% patients improved over time and 53% worsened. Only 33% were able to work.

F Friedberg (Stony Brook) had done a cross sectional study of support group attendees looking at the benefits and problems encountered. In general subjects had found the group experiences helpful, but somewhat surprisingly active support group members reported greater symptom severity and less illness improvement than inactive members.

Level of occupational disability comparing a maximal exercise stress test and two self report disability measures was presented by J.Nijs (Brussels, Belgium). The associations were too weak to predict occupational disability, and more work is required to establish valid methods of assessment.

The Phase III clinical trial of Ampligen v placebo in CFS was discussed by D.Strayer (Philadelphia PA). The trial involved 234 severely affected patients. 400mg ampligen or placebo equivalent in saline infusion was given IV twice weekly for 40 weeks. Exercise treadmill duration was improved two-fold over placebo. There were no significant differences in laboratory parameters. Ampligen has provided the most promising results compared with other drugs tried such as galantamine, antidepressants and corticosteroids.

L.Jason (Chicago) compared and contrasted the various case definitions for CFS/ME. The London ME criteria select a more symptomatic group of individuals than the Fukuda criteria. Using the Canadian criteria, there is less psychological morbidity included and more physical and functional impairment. There are more symptoms relating to fatigue and weakness coupled with neuropsychological and neurological symptoms.

Fatigue was defined by J.Jones (CDC,Atlanta) as a regulatory or protective process in illness – a component of illness behaviour. It is controlled by antagonistic activity of inhibitory/activating systems in the brainstem. Mediation of immune responses occurs in illness and prolonged illness maybe due to exuberant or inadequate host responses. Damage is a trigger for immune response. He described also the effects of unconscious self regulation which included psychological and philosophical components. Acute sickness causes a response to primary altered self, and repeated episodes can lead to conditioning and produce effects such as chronic fatigue. Targetting the prevention of the circle of CFS seems appropriate for further research and treatment.

K de Meirleir (Brussels, Belgium) described CFS as an immuno-vigilance disorder, with host/environmental problems. The initiating factors are heterogeneous. There is an abnormal level of apoptosis, and the nuclei cannot ingest all the resulting fragments. RNaseL fragments then accumulate. Some thyroid suppression may occur without abnormalities in TFTs. PKR activity is increased along a continuum. A number of patients are IgM positive to intestinal pathogens, and when treated with antibiotics (eg ciprofloxacin) these patients show a 74% decrease in elastase and 58% clinical improvement over 3 months. Therapeutic strategies should include: restoration of immune competence, elimination of micro-organisms, restoration of hormones, restoration of normal intestinal flora and decrease of PKR activity.

The next clinical segment was devoted to issues around autonomic dysfunction. C.Lapp (Charlotte NC) gave an overview. He described the autonomic nervous system as controlling all the automatic functions in the body. He gave background to the original research by P Rowe et al and described the various types of orthostatic intolerance: Orthostasis, Postural Orthostatic Tachycardia Syndrome (POTS), Symptomatic Orthostatic Tachycardia (SOTS) and Neurally Mediated Hypotension (NMH). These conditions can be distinguished using tilt table testing. Various causes were outlined including: low blood volume, low total body water, CNS disorder, venous pooling. Possibilities for managing orthostatic intolerance include: volume expansion (salt and water), fludrocortisone, midodrine, beta-blockers, SSRIs, amphetamines, IV fluids and erythropoietin.

D.Bell (Lyndonville NY) discussed his findings relating to volume depletion and ADH in CFS. He described how polyuria and thirst maybe early symptoms in CFS. He reviewed his original study where red blood cell (RBC) mass, plasma volume and circulating volume were found to be significantly depleted in CFS patients studied. RBC mass is probably the most important issue. 73% of patients studied had low RBC mass. If blood volume is low, ADH should rise but if levels are low

there is increased osmability leading to low BP, nausea and hypoxia. Some patients in the past have responded to various IV infusions (eg γ -globulin, Vit C, antibiotics) and it is probable that this has been a "placebo" type response just due to increasing blood volume. Bell has used daily one litre IV saline infusions with some encouraging results in 17 patients. Two stopped treatment, five had slight improvement and 10 had good to excellent results. However serious risks such as line infections maybe encountered.

Therapy using erythropoietin was then addressed by B.Hurwitz. He described patients who suffered from episodic hypotension with a tendency to syncope when upright. These patients had a lowered cardiac ejection fraction and decreased cardiac tone. Lowered blood volume was associated with mildly elevated ESR, suggesting the presence of a heightened inflammatory process. Earlier studies using volume expansion had produced some good results, but adding erythropoietin has the potential to improvement in non-responders. Erythropoietin is produced in the kidneys and stimulates the production of erythroid cells. A deficiency leads to normocytic anaemia. Production is modulated by the sympathetic nervous system. His hypothesis focussed on treating with erythropoietin to improve cardiovascular and autonomic symptoms and thus improve quality of life. Ongoing research with 94 patients to test this hypothesis was outlined, and involved three subcutaneous injections weekly. Supplemental iron and salt were included. There is one year left in this promising study.

Discussion as to whether CFS and chronic Lyme disease are the same was addressed by S.Schwarz (Tulsa OK) and an excellent overview of the research into diagnosis and management of Lyme disease was presented. It seems still unclear as to whether fatigue after Lyme disease is a form of CFS or is due to unresolved infection with persisting immune dysfunction. Antibiotic treatment has not conclusively been shown to be effective in randomised trials, but this maybe due to the choice of antibiotics used. There may also be different varieties of Lyme in different parts of the world.

N.Klimas (Miami,FL) AND L.Jason (Chicago) discussed the subgrouping of CFS by various means taking care to avoid the tendency to generalise. CFS represents a heterogenous syndrome. Subgroups can be based on biological markers; duration, severity and symptom complex (predominantly cognitive or associated with pain), and acute versus slow onset. There are a number of overlapping subpopulations with symptomatology relating to the immune system, the autonomic system, HPA etc. all within the chronic fatigue complex. Subgrouping could also been done looking at gene expression. Finding distinct sub-populations has clear clinical implications by defining groups for targeted intervention. Objective measures are needed for this

approach and can include issues such as: neuroendocrine (hypocortisolism), autonomic (orthostatic intolerance), immune (cytokines, cell function), cognitive (PASAT), psychological co-morbidity (SCID), Physical exam findings (+ve Romberg, hypermobility), documented infection at onset etc. Subgrouping is the key to understanding how CFS begins, how it is maintained, how medical and psychological variables influence its course and how it can be prevented, treated and cured.

A lawyer, T.Bush (Madison WI) provided some good useful advice for doctors who have to produce reports determining disability impairment. An objective opinion of the level of function is needed. Patients may be turned down for disability benefits if there is no medically determinable impairment. There is considerable difficulty in proving one cannot do a sedentary job. Doctors must record detail in the medical records such as distance patient can walk, time able to stand etc. Including lab results can help in explanantion. It is not often possible to perform a work simulation. If there is past history of annual physical examination, previous capacity etc this should be included and there needs to be stress on the issue of "changed health".

A panel discussion/advocacy workshop was led by N Klimas (Miami FL). Various points were noted. There is risk of defining the illness behaviourally if research is not supported. Physicians' voices carry more weight than those of patients. The WHO has reclassified CFS as a neurological illness rather than psychological. The word "fatigue" however is still very unpopular and unhelpful and many felt, outdated, but it was unlikely to be changed in the immediate future. Continuing action for recognition and support was strongly supported.



WORKSHOPS

EXERCISE WORKSHOP

Because studies have shown that exercise can be beneficial in CFS a full session was devoted to an exercise workshop, and the first presentation was by exercise scientists S.Stevens and C Snell who discussed strength and conditioning in CFS. Emphasis was on forgetting the "Athlete Model". Aim should be to focus on improving quality of life and developing coping tools to manage the illness and restore function. They described two types of patients: the roller coaster and the activity avoider, the latter compounded by the fear factor. When planning a strategy, questions need to be asked such as issues of post-exertional malaise (immediate and delayed), recovery responses including length taken to recover etc. The aim should be to pay back oxygen debt with rest. Fatigue after exercise is due to oxygen deficiency. A programme of "analeptic exercise" should be initiated which trains the short term system, restores

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functional movement and improves range of motion and strength. Appropriate exercise should be included in the daily routine and payback involves focussed breathing (3 seconds in/3 seconds out). The programme needs to be justified and the therapist needs to understand the physical limitations of the illness. The progressions should include:

- 1) Stretching/strengthening
- 2) Stretch with resistance training
- 3) Dose controlled interval training and
- 4) Maintenance.



C.Lapp (Charlotte NC) discussed interval exercise in CFS/FM. He pointed out the fact that even minimal exercise can trigger a flare of symptoms, while there is a fantasy that exercise is the cure. People often get sick when the patient aims for the anaerobic threshold (AT). This threshold occurs much sooner in those with CFS than healthy people. The relationship of energy expended to impairment is used to measure the impairment, the AT can be worked out and that should be the maximum time and level that the patient exerts. Interval exercise can slowly improve fitness. A study example was given showing how using repeated bursts of 3 minutes of exercise followed by 3 minutes of rest over one hour led to benefit. These patients were quite severely affected and none relapsed.

J.Hoffman has developed an exercise and conditioning programme for those with FM. Aerobic fitness, flexibility and strength are all decreased due to lack of activity rather than the disease. Four steps were outlined to improve muscle fitness:

- 1) Alignment of body, breathing and relaxation
- 2) Flexibility by stretching with rest and relaxation between moves.
- 3) Resistance training to build core strength (maximum of twice weekly, and avoidance during relapse)
- 4) Endurance training for 20 minutes 2-3 times weekly of low to moderate intensity.

Repetition and holding poses should be avoided. During relapses there should be emphasis on reducing level of exercise, decreasing endurance, hydrating well and using warmth and medication. The patient should be encouraged not to stop altogether. Patient needs to constantly "hold back" to avoid the roller coaster crash and burn effect. Exercise needs to be fun with extrinsic rewards and group adhesion.

COGNITIVE BEHAVIOUR THERAPY WORKSHOP

F.Friedberg (Stonybrook) explained the importance of understanding and utilising CBT in the management

of CFS. He gave a detailed overview of his approach pointing out that many CFS patients often had poor coping styles leading to greater illness severity. For improvement to occur there needs to be sustained lifestyle change, with efforts equal to that seen in investments in alternative treatments. If a full programme is undertaken for 6 months, there is likely to be at least 20% improvement and 50% is possible. Relaxation, sleep, anger management, pacing with graded activity, easing into pleasurable feelings and enlisting support networks are included in Friedberg's protocol.

E.Van Hoof (Brussels, Belgium) continued with this workshop presentation and stressed that there should be an aim to change cognition and behaviour to improve quality of life and allow life within the constraints of the illness. She utilises a phase approach, which includes: explanation and understanding, illness awareness and shift of locus of control, stabilization based on behavioural therapy, restructuring and re-integration. Patients often improve by not focussing on bodily symptoms and by setting realistic goals.

Twelve weeks of CBT group therapy is utilised by M.Segota (Miami FL) taking a stress management and relaxation (SMART) approach aiming to interrupt the CFS - stress - illness continuum. In each 2 hour session, 90 minutes is spent on CBT and 30 minutes using relaxation and imagery. The primary goal is to provide cognitive skills, optimize activity, relieve anxiety etc. The sessions cover stress management, cognitive restructuring, resolving interpersonal difficulties, self esteem enhancement and personal fulfilment. Working in groups has been shown to be cost effective.



POSTERS

Over 50 papers were displayed and while it is not possible to summarise them all in detail, important points will be covered.

EPIDEMIOLOGY

Subgrouping in CFS was addressed by K.Coradi (Chicago). Those with no evidence of ongoing infectious or inflammatory processes had the greatest level of physical disability, while those with evidence of ongoing infection were at increased risk of psychiatric co-morbidity. Minority groups were more likely to be in the group suggesting ongoing infection.

In a nine year follow up of Danish patients presented by M.Anderson (Copenhagen,Denmark) there was no evident significant overall improvement in 35 adults with CFS. There was evidence of severe disabling illness, not typically associated with depression or hysteria.

In Norway, a population-based registry for patients with ME/PVFS has been established and reported on by S.Kreyberg (Oslo,Norway), and this is a useful tool for understanding and intervention, and provides opportunity for choice and understanding for those with the illness.

A.Morris (Chicago) had used the Geographic Information Systems (GIS) to allow investigators determine associations between environmental risk factors and location in CFS. This seems a promising method for these studies.

S.Torres-Harding (Chicago) compared the prevalence of fatigue among English and Spanish-speaking Latinos, who appear to be 2 distinct sociodemographic groups. The English speakers were found to have higher levels of overall fatigue, higher physical fatigue and were more likely to have chronic fatigue. M. Njoku (Chicago) also found that different coping strategies were employed by different ethnic groups (African American, Latino and Caucasian) and are related to disability and fatigue severity. Cultural practices, resources, life experiences etc may influence the coping strategies.

A study looking at the biopsychosocial model of post infectious fatigue in adolescents may help to explain the aetiology of this subtype according to R Taylor (Chicago).

SPECIALISED CFS CENTRES

Five clinical networking centres for CFS patients were established in Belgium, and although this has proved to be far from adequate, G Moorkens (Antwerp, Belgium) showed the concept is excellent and future programmes should follow.

E Van Hoof (Brussels,Belgium) discussed the findings regarding patients attending a tertiary CF clinic. 80% are diagnosed with CFS according to the CDC criteria. Only 5% of these were not given a diagnosis of CFS. RNaseL was found to be elevated in 92% of the CFS patients.

PHYSIOLOGY

Autonomic dysfunction is identifiable with the use of a tilt table and this should be utilised as one of the assessment tools for those with CFS, according to C Lapp (Charlotte NC). There is a high rate of positivity in CFS particularly those who have symptoms suggestive of orthostatic intolerance. He has shown that the symptoms do predict the likely outcome of tilt table testing.

Coagulopathies in relation to CFS and other chronic illnesses may have a common aetiology due to immune system activation of coagulation (ISAC). Increased plasma fibrin deposits on capillary walls and also increases plasma viscosity, decreasing blood flow. Low

dose heparin therapy (not warfarin) decreases thrombin generation leading to an anticoagulant environment in the capillaries, but specific protocols do need to be developed. H.Harrison (Phoenix AZ) provided further studies on coagulation issues showing an increased prevalence of abnormalities in inherited thrombophilic and hypofibrinolytic proteins in those with CFS and HHV6 infection. Patients may need to be monitored for overt thrombotic phenomena.

Autonomic function in MCS patients and controls was compared by analysing heart rate variability by K.Yoshiuchi and H Kikuchi(Tokyo,Japan). Spectral analysis showed consistent differences in autonomic function between the patients and controls both while awake and asleep. CFS also appears to influence α -2 heart rate variability before and after exercise, while POTS appeared to alter it in the opposite direction.

R.Shoemaker (Pocomoke.MD) outlined a number of immunological and neurochemical pathways involved in the pathogenesis of CFS and proposes the study of the physiology of biotoxins as a potential treatment approach.

IMMUNOLOGY and MICROBIOLOGY

G Quintana (Barcelona,Spain) produced results on a series of CFS patients showing that 93% had a positive RNaseL protein which correlated positively with RNaseL activity and monocyte elastase activity. This suggests that elastase maybe implicated in the development of CFS. New pharmacological strategies looking at elastase inhibitors may prove worthwhile.

D Racciatti (Chieti,Italy) confirmed the potential role of immune activation in precipitating and perpetuating CFS. Further research looking at specific immunological markers may help identify sub groups of patients, and this may improve the chances of identifying pathological mechanisms in this disease.

Guidelines have been produced to define if there is a causal relationship between development of fatigue states and immunization. K.Kohl (CDC) presented this work which included recommendations for testing usefulness and clinical trials.

A.Chester (Washington DC) has found that functional endoscopic sinus surgery is a successful treatment for CFS associated with rhinosinusitis.

The presence of methylobacteria in the bloodstream as a possible relationship with CFS needs further addressing according to L Lindner (Bryan,TX). The importance of these bacteria in health and disease is yet to be determined, but he raises the possibility of further research.