

# REPORT

ON THE 8<sup>th</sup> INTERNATIONAL IACFS CONFERENCE -  
10<sup>th</sup> - 14<sup>th</sup> JANUARY 2007

HELD AT THE BAHIA MAR HOTEL, FT. LAUDERDALE, FLORIDA, USA



BY CLARE BOLD



TRUSTEE AND FUNDRAISER, FIBROMYALGIA SUPPORT GROUP FOR  
SURREY AND SUSSEX



*The Conference Hotel, the Bahia Mar*



*Fort Lauderdale Beach, which was just across the road from the Conference hotel*



*Jo and Clare were awarded Scholarships by PANDORA to take part in the Advocacy and Leadership Program*



*Nancy Gordon, Rebecca Artman, Marly Silverman, Yvette Taylor and Jo Fisher*



*Patient Conference Delegates - Eva, Jana and Kathy*



*The hotel Ballroom where the main Conference took place*

## **ACKNOWLEDGMENTS**

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Grateful thanks go to the Group's Funders who made the trip possible, plus the very generous PANDORA (Patient Alliance for Neuroendocrine-immune Disorders Organization for Research and Advocacy), who co-sponsored the Conference, especially Marly Silverman, Founder and President of PANDORA. Jo and Clare were awarded Scholarships by PANDORA, so that they could take part in the 2007 Advocates Extraordinaire Advocacy and Leadership Program, and PANDORA also contributed to their accommodation costs.

Thanks must also go to all the people we met during both the Patient and Professional Conferences. It was great to share experiences and coping strategies and to socialise with the many patients with Fibromyalgia, CFS, ME and other related conditions and fantastic to see so many top doctors, specialists and researchers from around the world coming together to participate in the Conference. We made many new contacts and friends which will further our aims as a Group, thus increasing our power and impact.

Many thanks too to our team of proofreaders and family and friends who have helped with typing and checking this Report.

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## ***Foreword***

***By Jo Fisher***



I hope that you enjoy reading this Report and find the information contained in it useful. There is a great deal to tell you about the Conference. The presentations we heard from doctors from all over the world were very interesting and also very encouraging. It is great to know that all this research and work is being done to find out more about ME, CFS and Fibromyalgia.

There were approximately 28 different countries represented at the Conference, all working to understand these debilitating conditions. It will be these doctors that go back to their own countries and share all the information they have learnt and discussed at the Conference. This will hopefully encourage even more research in the future to help patients and Healthcare Professionals alike.

I was able to network with many of the top doctors, some of whom have agreed to work with the Group and maybe even come over to the UK for a Conference in the near future, which would be wonderful. There was also an Exhibition Hall and I picked up lots of literature from there too, and made several contacts, which may bear fruit in the future.

It was great to talk to other sufferers from different countries to see how they were coping and what difficulties they experienced, what treatments were available to them and how they were perceived in their countries by the Healthcare Profession and Government Bodies as a whole. It is interesting to see that we all seem to have similar problems but some have far better treatment facilities than others.

I found it really hard seeing and speaking with many of the children and teenagers affected by these conditions and to listen to the parents who were desperate for something to help their children. Many have taken positive steps and parents have got together and started a support network for themselves and their children. The networking that goes on at these Conferences is so important.

I am really grateful to the IACFS for being able to bring all the Advocates from around the world together to meet and discuss issues and to learn from each other so they can go back to their own countries and spread the word. It was great to see the unity amongst the doctors and total commitment in wanting to find the answers to the questions about these conditions and their underlying causes. It helps to know that things are being done and they are getting somewhere so we have something to feel really positive about and ever hopeful of further treatment options in the future.

## ***Introduction***

***By Clare Bold***



For those who don't know me, I was diagnosed with chronic Fibromyalgia in February 2005 and shortly afterwards had to give up my career as a Qualified Management Accountant. The Fibromyalgia Support Group for Surrey and Sussex helped me enormously, in learning to live with my condition, introducing me to other patients, and giving me the opportunity to try new activities such as yoga. I became a Trustee of the Group in November 2005 and help with submitting Funding Applications and some Finance issues.

I was truly honoured to be offered the chance to represent the Group at the 8<sup>th</sup> International IACFS Conference in Fort Lauderdale, Florida, USA, in January 2007. For someone who had only ever flown as far as Ireland before, even the trip across 'the pond' was a huge adventure for me!

There were actually two Conferences over a five day period. The first, lasting two days, was a Patient Conference, for sufferers of Fibromyalgia, CFS/ME and other related illnesses, and the second, was a Professional Conference for Doctors and Healthcare Professionals.

Jo and I had been awarded Scholarships by PANDORA, so that we could take part in the 2007 Advocates Extraordinaire Advocacy and Leadership Program, so on the first day of the Conference we were committed to attending presentations and workshops designed to improve our skills in Advocacy and Leadership. These sessions proved to be very useful and I think the skills we learned will help the Group tremendously.

The second day of the Conference included new science, research and treatment options, family issues and paediatrics and challenges and risk factors for patients.

The Professional Conference was aimed at the Medical Profession, and covered Fatigue, Sleep, Clinical Trials, Pain, Genetics, Immunology and related topics.

Each day was at least twelve hours long (so we had no time at all for sight-seeing!) and there were up to four presentations/workshops taking place at any one time (plus the Exhibition Hall) so Jo and I had to carefully assess which sessions to attend, so as to gain as much as we possibly could from the Conference.

I hope that you will find the Report informative and interesting to read.

*Section A*

*Patient Conference*



## *Chapter 1*

### *Advocates Extraordinaire Program*

On Day 1 of the Patient Conference Jo and I attended special workshops designed for the Leadership and Advocacy Training Program, which enabled us to gain extensive knowledge, thus empowering us as advocates and giving us some useful information to bring back to the UK.

#### **Fundraising**

The first main workshop of the day was ‘Fundraising Fundamentals’ by Joanne Nowlin Davis. She talked about ‘The 7 Steps to Successful Fundraising’, by Ann Fritschner which gave some useful tips on planning and budgeting. She also talked about what an organisation ‘needs’ ie. what is essential for its survival, and what it ‘wants’, ie. if it could have anything at all, and she stressed the difference between the two.

For organisations such as charities, *need* is the most important, as it is the bottom line to keep the charity up and running and the services flowing to the people you are serving. Achieving funding is vital as without the charity would not be able to survive.

Joanne went on to talk about how to conduct a ‘SWOT’ analysis, ie. identifying an organisation’s strengths weaknesses, opportunities and threats, and how to build a plan and budget from this, also taking into account past performance.

It is important to establish whom to approach for funding and Joanne broke down potential donors into 4 tiers, looking at the advantages and disadvantages of each. She talked about ‘Maslow’s Hierarchy of Needs’ which analyses the reasons people give, and stressed the importance of an organisation making it easy for people to donate to and also making it *fun* to give. Her talk concluded with a session on how to thank people, for example, printing names in the magazine/annual report, or the right to anonymity. Some funders require us to acknowledge their sponsorship, and in these cases we are obliged to print their logos and say ‘supported by’ on our magazines/letterheads etc.

#### **Media Training**

We attended several workshops designed to train us on how to approach and speak to the media. Jo is already an expert in this field, having done a live television interview and several live radio interviews, plus numerous press interviews in the past, but it was all very new to me. I have, however, already put some of the skills I learnt into practice by giving a 45 minute interview for a yoga magazine. The journalist was looking for a ‘real-life’ story of someone who has Fibromyalgia and how yoga has helped them.

The first media training session was with Martin Kramer of Dezenhall Resources, and was titled 'How to Convey your Advocacy Message to the Media.'

Martin talked about what not to do when talking to the media, ie. be unprepared and give inaccurate information, use acronyms and jargon, cite irrelevant good news, pick fights that you can't win, introduce/repeat the negative and forget to deliver your message.

Instead he emphasised the importance of first impressions, and looking and sounding good. He talked about non-verbal communication, the importance of body language and also your eyes, voice and the way you dress. Non-verbal signals can easily override what you are actually saying.

Other recommendations were to be human, not perfect, to use layman terms, not to 'translate' for example by saying 'what I mean by that is', and to acknowledge concern for people with Fibromyalgia, as care and empathy will foster trust and credibility.

Martin said the key to getting your point across is to have a 'message' and to repeat it over and over so that it sticks with the interviewer. He said a good message should be functionally defensible, personally relevant (and a local angle will always grab a reporter's attention), deliverable within 15 seconds, must connect emotionally with core values, be simple enough to make common sense and it must also be quotable.

Following Martin's presentation were two practical workshops, with several brave volunteers being interviewed on camera and then the interviews were replayed for all advocates to comment on their strengths and weaknesses and what went well and what didn't work so well. The sessions and interviews were led by Diana Mohoreanu and Martin Kramer from Dezenhall Resources. These interviews really highlighted the importance of body language, eye contact and facial expressions and the necessity for getting your message across, despite being bombarded with questions from the interviewer.

### **Brain-Storming and Strategy Meeting**

For the final session of the day we were split into about a dozen groups, each with one particular topic to discuss. Jo and I joined the 'International Issues' group, as we had a special interest in that we were representing the UK at a Conference in the USA. We started by going round the table introducing ourselves, saying who we were, where we were from and what we did etc. and it soon became clear that we were sitting with some very significant individuals! We were fortunate to be able to discuss some very important and interesting international issues in a group of about ten, including some of the IACFS Board Members, Dharam Ablashi (who actually discovered the Human Herpes Virus 6, HHV-6, in 1986!) and Birgitta Evengard, and our group leader was Rebecca Artman of PANDORA.

This was a great brain-storming session where we had to come up with a list of the top ten most important international issues regarding CFS, ME and Fibromyalgia. We discussed the importance of 'all singing from the same hymn sheet' and knowing what research and development work was going on in each country, as we had representatives at the Conference from the USA, UK, Sweden, Norway, Japan and Spain, to name but a few.

At the end of the session we listed our top ten international issues on a flip-chart. The other groups, who were discussing a wide range of topics from gender issues to paediatrics and definitions of fatigue, did the same. Each group's sheet was pinned up on the wall and we had a short break to walk around and look at them. We had coloured stickers to stick on the two issues we thought were the most important for each group.

After the break we got back into our groups, reclaimed our flip-chart sheet and discussed the two issues the other delegates had ranked as the two most important. From this we had to discuss what we thought was the most important international issue and then how we would start to resolve the issue and address some of the problems associated with it.

Our group's main priority was the development of an international platform for representatives from each country to discuss research and development and to share information and resources. We agreed that a good way to do this would be to build a website, which would host relevant articles and research papers and also provide discussion forums for both patients and medical professionals.

The ideas that emerged from the brain-storming session were put to the IACFS Board after the Conference that day at their evening meeting and the following day Jo and I were called to one side by Rebecca Artman from PANDORA, who told us that the IACFS Board had taken on board our main international issue and our plan for a web-based platform of sharing between countries and had decided to take the idea forward, with the members of the discussion group being initial representatives from their countries. This was fantastic news, as it not only showed that we were being listened to, but that our ideas were being transformed into action, and we really were making a difference and participating in change.

## *Chapter 2*

### *Cocktail Reception Lecture*

#### *Effective Pain Management in CFS and Fibromyalgia – Dr Jacob Teitelbaum*

Jacob Teitelbaum started his talk by defining pain. He said that pain is the body's way of telling us that something is wrong and needs attention, like a warning light on a car dashboard. He went on to say that it is, however, not acceptable for anyone to be in pain and that there are ways of managing and controlling pain. In an analogy with a blown fuse, Dr Teitelbaum explained how with Fibromyalgia and CFS it is not simply a case of replacing the fuse without getting to the root of the problem, otherwise the fuse will just blow again.

Dr Teitelbaum uses the acronym 'SHIN' in treating pain, where:-

S	means SLEEP
H	means HORMONES
I	means INFECTION
N	means NUTRITION

He stressed the importance of getting 8-9 hours sleep per night, controlling hormones, particularly thyroid hormones, controlling infections, for example yeast, and ensuring good nutrition in managing Fibromyalgia and CFS symptoms.

In various studies, he has found that 99% of patients have shown significant improvement in their symptoms by following his plan based on 'SHIN'. He has written several books including his latest, 'Pain-free 1-2-3' and sells nutritional supplements via his website '[www.vitality101.com](http://www.vitality101.com)'. He does not take any profit from the sale of his books and supplements and donates his royalties to charity.

Dr Teitelbaum suffered with Fibromyalgia and CFS himself, which was triggered by a bout of the flu in 1975, and he actually ended up homeless for a year. But, with considerable stoicism, research and hard work, he is now in remission and is able to live a normal life helping patients and also educating doctors. He admitted though that he has to be very careful, listen to his body, and follow his own 'SHIN' plan, otherwise he will be in danger of 'blowing a fuse' once again. The fact that he has 'been there' inspires confidence in his approach to treatment and he demonstrates great empathy and understanding.

Fibromyalgia and CFS is an energy crisis. You are expending more energy than you can make, says Dr Teitelbaum. Triggers can be trauma, pregnancy, the menopause, stress, moving house, infection, bereavement, changing jobs, redundancy etc. or maybe several of these at the same time.

Dr Teitelbaum said the hypothalamus is often the first area to be affected. This controls fourteen important body functions including sleep, hormones, temperature regulation, blood pressure and pulse. Using his analogy of the fuse-box, he says that you can turn the circuit breaker back on, but you need to fix the

underlying problem so that you don't blow a fuse again. His motto is "Don't do anything that doesn't feel good" and he now puts his energy into activities that he enjoys.

He said the best place to start is with sleep, making sure that you get a good 8-9 hours per night. He was keen to stress the importance of the body's own ability to heal itself, and said to listen to your body and what it needs. Growth hormone, which regulates pain levels and body weight, is produced during deep sleep, so those of us not getting enough deep sleep can have problems with increased pain and weight gain.

Thyroid dysfunction is also common in Fibromyalgia and CFS patients, even if blood tests come back 'normal'. Using the analogy of shoe size, Dr Teitelbaum demonstrated that you have to be in the bottom or top 2.5% to be considered 'abnormal', which would equate to a normal shoe size of say 4-13. If a man was wearing a size 5 pair of shoes he would be suffering a great deal but the size is in the 'normal range' so he would not be seen to have a problem. We do not normally know what our test results would have been before we became ill, so we do not have anything to compare with to establish what is 'normal' for us.

Dr Teitelbaum recommends his nutritional supplement CORvalen (D-Ribose) for the treatment of Fibromyalgia and CFS. It is equivalent to taking 35 different supplements per day and more details can be found on his website. In trials he has found that 91% of patients have a significant improvement in their symptoms. For muscle pain in particular he suggests the 'SHIN' approach, and for neuropathic pain vitamins B12 and B6, anti-epileptic drugs such as Gabitril, Gabapentin and Pregabalin, and Lidoderm patches and pain-killing gels for topical relief. Studies have shown that Vitamin B6 and Armour Thyroid can help carpal tunnel syndrome pain within just 6 weeks. For arthritis pain he warned against NSAID use but says to increase your intake of fish oils and take MSM and Glucosamine supplements. Migraines are often caused by food allergies, so it is important to cut out foods that may trigger an attack. He has found that Vitamin B2 and also Magnesium has decreased migraines in 67% of cases.

He concluded that Fibromyalgia, pain and CFS are now treatable and that patients should explore his suggestions as we will not get any Brownie points for suffering!

## *Chapter 3*

### *What's New in CFS and Fibromyalgia Science, Treatment and Demographics*

Dr Nancy Klimas introduced the speakers in this session and mentioned that there were 300 patients in attendance (which is three times the number at the last IACFS Conference) and over 250 professionals.

Dr Hirohiko Kuratsune, from Japan, talked about CFS being a big economic problem for society. His research team have discovered bio-markers for the diagnosis of CFS and from this have developed a test which can distinguish between patients with and without CFS. Dr Birgitta Evengard has also found differences in brain function in those with CFS. Although patients can show normal results in neuro-psych testing, research has shown that brain function in CFS is different during cognitive work.

The CFS brain was said to be similar to the ageing brain. The older we get, the brain needs to draw from more areas to do a task satisfactorily. The brain works as a network and Birgitta used the analogy of a rubber band to explain the theory. A fresh rubber band will stretch and then snap right back but an older one will be more brittle and will need more work to wrap it around something successfully and it will not spring back as well as a new one. The CFS brain requires more resources to perform the same tasks as a normal brain.

Dr Kenny De Meirleir talked about the gastrointestinal system and said that this is where most mechanism in CFS start. Research has found in over a thousand patients that 80% had mal-digestion or mal-absorption problems and food intolerances or allergies. He believes that this is a predisposition to CFS. The gastrointestinal system is 70% of the body's immune system and has the surface area of a football field. Early antibodies for bacteria, toxins in the blood and increased heavy metals, such as mercury and nickel, have been found in CFS patients. Dr De Meirleir mentioned research that had shown that 57% of patients had elevated levels of nickel in their blood. It was also mentioned that the gut is also rich in serotonin, not just the brain, and therefore SSRI medications can sometimes help in CFS.

Dr Leonard Jason was impressed by the Conference and the number of people working together. He emphasised how important it was to have a good structure and for the people to take on research and to fill the gaps and how this helps the field of science. He also highlighted the economics of the illness and the associated indirect and direct costs to the economy.

Dr Dharam Ablashi went on to talk about the HHV-6 virus and its discovery in 1986. It was originally thought to be one virus, but it has now been established that there are two strains – A and B. Strain A is more prevalent in CFS, Fibromyalgia and MS, and B is commonly found in epileptic patients. But, in Japan, only B is present, and in Africa 37% of children have the A virus and the rest have type B.

## *Chapter 4*

### *Family Issues and Paediatrics*

Dr Leonard Jason and Dr Dave Bell introduced the session on Paediatrics which focused primarily on the new paediatric case definition, which has been produced by a working group over the past six months. There are five CFS symptom categories which must be present in order to diagnose paediatric CFS:-

Post-exertional malaise, unrefreshing sleep or sleep disturbance

Myofascial pain, joint pain, abdominal pain and/or head pain

Two or more neurocognitive manifestations

At least one symptom from two of the following sub-categories: 1. Autonomic manifestations, 2. Neuro-endocrine manifestations or 3. Immune manifestations.

The diagnosis can be made after three months of persistent or relapsing chronic fatigue that is not a result of exertion, is not substantially relieved by rest and results in substantial reduction in previous levels of educational, social and personal activities.

This new paediatric case definition should lead to more appropriate identification of children and adolescents with CFS. A paediatric health questionnaire has been produced, with adult and child versions to be completed jointly by the child and/or parent/care provider. Exclusionary criteria include past and present psychotic disorders of any variety, current anorexia or substance abuse. Treated depression is not exclusionary.

Dr Elke Van Hoof said that as scepticism is often associated with a diagnosis of CFS, parents may be accused of neglect or even abuse. A case study indicating the mistrust and dismissal experienced by some families illustrated this and tragically Munchausen by proxy can be mistakenly diagnosed.

Jo Fisher attended a discussion group with parents and children/adolescents diagnosed with CFS and Fibromyalgia. She found it difficult talking with the parents and children affected by these illnesses and the lack of support that they receive. On returning to the UK she has investigated the possibility of extending the Fibromyalgia Support Group for Surrey and Sussex to include support for young sufferers and their parents. She has met with a rheumatologist who specialises in the treatment of children with these conditions. He has said that there is currently little support for parents and children with these conditions in the UK which has further fuelled Jo's desire to reach out to this neglected patient group and we hope that we will soon have the necessary policies and procedures in place to meet their needs.

## *Chapter 5*

### *Exercise Challenges for the Fibromyalgia and CFS patient*

Dr Chuck Lapp talked about exercise for patients with Fibromyalgia and CFS. He said that it is a fantasy that vigorous exercise helps these conditions, but that graded exercise can be very beneficial. In a study he conducted with Dr Dave Bell, thirty one subjects were observed after using exercise bikes. The exercise caused 75% of the group a flare-up in their condition which lasted on average nine days, although twelve people flared for more than twelve days. They published these results and showed them to insurance companies to prove that exercise is not always good for Fibromyalgia and CFS sufferers.

So, how much exercise *can* patients do without adverse effects and triggering a flare?

The key is to look at the 'Anaerobic Threshold' (AT). This is the point at which the heart and lungs can no longer get enough oxygen to the body, the tissues and the muscles. Even trained athletes would feel aching and tired at this point and would have to stop. This point is established by asking a patient to ride an exercise bike, wearing a special mask which measures how much oxygen they breathe in and how much carbon dioxide they breathe out. The harder you exercise the more oxygen you need and the more carbon dioxide you breathe out. When the carbon dioxide you breathe out reaches the same level as the oxygen you are taking in you have reached the AT and cannot get any more oxygen into your body. In Fibromyalgia and CFS patients Lapp and Bell found that the oxygen capacity is much lower than normal and also the AT is reached much earlier, typically after 3-5 minutes exercise. They found patients to have near normal strength but their stamina was much lower.

They therefore recommended that patients exercise for no more than four minutes. The heart takes around five minutes to turn around all the blood in your body, so a five minute rest should then follow, and perhaps another four minutes of exercise. This kind of interval training seems to work best for those with Fibromyalgia and CFS. Dr Lapp acknowledged that patients have good days and bad days, so suggested that on good days you do several repetitions but on bad days just do it once.

Staci Stevens studied heart rate in Fibromyalgia and CFS patients, in an attempt to work out their maximum heart rate when exercising. However, this proved to be an unsuitable measure as most patients are already deconditioned, so by the time they get up out of a chair and walk a short distance their heart rate may already be well over one hundred beats per minute. Dr Lapp therefore concluded that the interval method is a much more effective measure.

Dr Clapp, a physical therapist, conducted a study of ten patients with CFS. None of them believed that they were able to exercise and some were wheelchair bound. He used the interval approach, where each patient walked on a treadmill for three minutes and then sat in a chair to rest for three minutes. They repeated this ten times, so each patient managed to do thirty minutes of exercise despite believing that they would be unable to do any. None of the patients relapsed afterwards, so it proved that interval training works.

Gentle warm-up exercises and stretching have also proved beneficial to Fibromyalgia and CFS patients and enables them to exercise for longer. Combining this with interval training and using the AT is the best approach for patients.

Janice Hoffman works with Dr Bennett at the Oregon Health Sciences University. She helps Fibromyalgia patients with increasing activity. Her approach is to start slowly and to build up gradually. Muscles tighten up and patients can become stooped, so the first step is to correct the abnormal pain postures by standing upright, with the shoulders back and the chin tucked in. Most Fibromyalgia sufferers are 'chest-breathers' and can therefore only take short shallow breaths. Janice teaches abdominal deep breathing which allows more oxygen to go to the muscles which reduces pain. Her regime also incorporates stretches, mainly of the upper body, and resistance exercising with light weights of just one or two pounds lifted above the head or strapped to the ankles for leg exercises. Later on she introduces some light aerobic exercise. Yoga and pilates are good forms of exercise for Fibromyalgia patients as they improve posture, flexibility, breathing and stamina. Exercise in water is also very therapeutic, and gentle swimming, walking or cycling are good choices for light aerobic activities.

Dr Lapp said it is important to ask yourself two questions after activity. How do I feel afterwards? And how do I feel the next day? He said if you have an increase in pain and/or fatigue after activity then to use the rule of 50% and to try only half the exertion next time and see how you feel afterwards and the next day. To cut back by 50%. He stressed the importance of keeping a daily schedule and sticking to a routine. It is usually when we break our routine that we have a flare-up. It is important to pace oneself, to set reasonable limits, and to schedule in rest breaks.

He concluded his presentation with the three major causes of relapse, which we should try to avoid, using the acronym 'SOS', for **S**tress, **O**ver-exertion and **S**leep deprivation.

Dr Kenny De Meirleir also spoke at this session on exercise. He said that many patients have 'kinesiophobia' which is a fear of exercise. This is understandable if your previous experience of exercise has left you in more pain and with greater fatigue than normal. But, exercise is important because during exercise endorphins and enkephalins are produced, which are the body's 'feel good' chemicals and natural pain-killers. But excessive exercise can actually lead to more infections and suppress the immune system.

Dr De Meirleir said that even on a bad day it is necessary to do a little exercise as it will help to eliminate the build up of lactic acid in the muscles and improve the use of glycogen, the body's energy which is stored in the muscles.

## ***Chapter 6***

### ***Risk Factors For People with Fibromyalgia and CFS***

Dr Leonard Jason led this session about the risk factors in Fibromyalgia and CFS patients. It was an open forum for discussion and many interesting questions were raised.

Some of the points mentioned in the exercise session were reinforced; for example, the Anaerobic Threshold is much lower than normal in Fibromyalgia and CFS patients, so it is important not to over-exert yourself. The 'break from routine' problem was also highlighted again. A patient asked about flying, as she always suffers a flare-up after travelling by plane. Dr Jason suggested pacing yourself before the flight, to pack gradually rather than rush at the last minute and do too much in the few days before travelling. He also said you could try muscle relaxant medication and oxygen therapy to help minimise a flare-up.

Over-activity before onset contributes to the development of Fibromyalgia and CFS and under-activity following onset contributes to its severity, disability and longevity.

A meaty discussion topic was about the effects of having Fibromyalgia and CFS and how this impinges on the condition itself. For example, the social losses, losing friends who don't understand why you can't do the things you used to be able to do and think that you are just making excuses when you say you can't attend an event. Eventually they stop inviting you! Many sufferers will become isolated or even house-bound. A large number will have to give up their jobs, or at least reduce their hours, which can cause a huge financial strain. They may have to claim social security benefits or claim on insurance policies, which has certain stigmas attached, and can be exhausting and stressful. Patients may also be up against doctors and physicians who know little about their illness and may even disbelieve them. Fibromyalgia and CFS are frequently misdiagnosed with primary psychiatric disorders. Heterogeneity is a risk factor because everyone is *not* the same.

Some depression or anxiety disorder has been correlated with CFS and in some studies has also been seen predictive of CFS. There is often severe stress at the onset of Fibromyalgia and CFS, but depression and anxiety may be as a reaction to the losses mentioned above and the change in lifestyle that the conditions impose.

It has been shown that a positive attitude is vital in aiding recovery. Self-help groups have been shown to be hugely beneficial to sufferers, but some studies have shown that people who attend such groups might find it more difficult to recover because they are 'wallowing' in their illness. Therefore positive self-help groups, where the emphasis is on education, and learning to manage and cope with the condition are the most helpful. Whilst it is good to meet with other sufferers and share experiences it is not beneficial to be negative and not want to get better.

## *Chapter 7*

### *Attendee Banquet and PANDORA Sandcastle Awards – With Keynote Speaker Dr Paul Cheney*

A banquet and award ceremony marked the end of the Patient Conference. Jo and I were able to attend thanks to PANDORA who sponsored us. This was a great social occasion and enabled patients to chat to each other and let their hair down, although most attendees by now, after two long intense days, were absolutely shattered! The PANDORA Sandcastle Awards were presented to the winners, including the following categories: - Lifetime Achievement, Outstanding Advocates, Pioneer Spirit, and Outstanding Fibromyalgia and CFS Physicians. Music was provided by a pianist and an opera singer.

After dinner and the Award Ceremony, Dr Paul Cheney spoke about diastolic (*this is at the resting phase of the cardiac cycle, when the heart is in a period of relaxation and dilatation, or expansion*) dysfunction in patients with CFS enhanced by tilt-echocardiography. In his study of ninety cases, with Dr Lucki, he began with the hypothesis that CFS patients have a disorder of cellular energy production which might, if it affected the heart, present as energy dependent cardiac dysfunction such as diastolic dysfunction with preserved ejection fraction. This could explain the rise in diastolic heart failure which is now over 54% of all heart failure admissions.

A preliminary age and sex-matched case-control study of ten CFS cases and ten normal controls was used to assess the sensitivity and specificity of a large set of echo parameters, especially diastolic parameters. The patients' readings were taken as they were lying on a tilt table at different angles, ie. a thirty degree and seventy degree head up tilt with five minutes of equilibration before each echo interrogation.

Following the preliminary study, a larger study of ninety patients from twenty nine states and four countries were evaluated in a national referral practice for CFS. The average age of the patients was 48.9 years. A history of hypertension was rare and only four were diabetic, with only one type I diabetic. Over 90% were disabled with CFS with many house-bound and an average length of illness of 17 years. 71% of the patients in the study were female.

Dr Cheney concluded that CFS patients exhibit evidence of diastolic dysfunction at a level well above that for control populations of the same age. Energy dependent diastolic dysfunction would appear to be a hallmark of CFS and supports the hypothesis that CFS is a syndrome of cellular energy deficiency. The tilt echo protocols provide an amplification of often masked diastolic dysfunction in those with CFS.

*Section B*

*Professional Conference*



## *Chapter 8*

### *Fatigue Session*

Dr Yasuyoshi Watanabe, from Japan, opened the Fatigue Session. He said that although a lot of people are suffering from chronic fatigue lasting longer than six months (more than one third of the Japanese population), there has been a lack of integrated research on fatigue. Everyone has experienced fatigue at some point in their life, but its molecular and neural mechanisms have not been studied in great detail, probably due to the complexities surrounding the causes of fatigue. However, we are all aware of how fatigue can decrease the efficiency of our work. It is of great value in our modern society to extensively analyse the causes of fatigue and develop the quantification methods on fatigue, for intervention of the methods and therapies with better recovery and avoidance of severe chronic fatigue. The economical gain will be huge if chronic fatigue is somehow cured. Almost all commercially available aids to recovery from fatigue are not proven by scientific and medical evidence, to Dr Watanabe's surprise and regret.

Dr Watanabe's team of researchers at Osaka City University Graduate School of Medicine organised an integrated research project on "The molecular/neural mechanisms of fatigue and fatigue sensation and the way to overcome chronic fatigue" under the control of the Ministry of Education, Culture, Sports, Science and Technology, Japanese Government from 1999 to 2005. The project was conducted by twenty six laboratories in universities and institutions and included: the elucidation of the brain regions and their neurotransmitter systems responsible for fatigue sensation and chronic fatigue, development of a variety of methods and scales to quantitatively evaluate the extent of fatigue, elucidation of molecular/neural mechanisms of fatigue in humans and animals, and the development of various methods or therapies for chronic fatigue.

More recently research direction has been to look for/develop foods and drugs to overcome fatigue and also to examine the environment; for example, air-conditioning, interior design, aroma, music, hotel rooms, offices and traffic. Fatigue is the problem of individuals, but also the problem of society, so we therefore need to investigate and analyse the social aspects of fatigue especially in modern city life.

Dr Nicole Porter from DePaul University talked about examining and distinguishing types of fatigue. The aim of her study was to examine the validity of the ME/CFS Fatigue Types Questionnaire (MFTQ) in assessing various types of fatigue that people experience. Research suggests that there are different types of fatigue that people experience in their lives, including post-exertional fatigue and brain-fog. However, current medical terminology does not differentiate between these fatigue types. The MFTQ was developed to address this problem in the study of fatigue, the objective being to survey a group of healthy individuals and those who have CFS, using the MFTQ, in order to evaluate its ability to differentiate different types of fatigue.

A survey including the MFTQ and other existing fatigue scales (Chalder fatigue scale, Krupp fatigue scale and Ray et al. fatigue scale) was administered to 200 undergraduate students at DePaul University, in person, and to 200 people with CFS who are members of CFS support groups in Chicago, IL and Madison

Winconsin by mail. The participants for both groups were anonymous. The data collected was analysed using factor analysis to differentiate various types of fatigue.

Results showed that in differentiating the types of fatigue that people experience there are *five types of fatigue*, currently labelled as:-

- (1) Molasses fatigue
- (2) Wired fatigue
- (3) Brain-fog fatigue
- (4) Post-exertional fatigue
- (5) Flu fatigue

By creating these new terms to characterise the different types of fatigue people experience, it helps reduce the complexity that surrounds the word 'fatigue'. Fatigue can now be expressed on more of a continuum, expressing different severities and symptoms. This helps understand and examine fatigue more thoroughly than the earlier categorical classifications that only explain a unidimensional fatigue as being present or absent, or of a certain severity. This will also help us to understand and evaluate fatigue associated with overlapping conditions such as Fibromyalgia.

Dr Elizabeth Maloney confirmed the link between CFS and high allostatic load. Allostasis is the maintenance of stability through change. Environment, trauma, stress, behavioural response, genes and developmental experiences all have an effect on the physiological changes leading to allostatic load. In her study 56% of CFS patients were found to have high allostatic load (females greater than males).

It was also found that those with CFS in this study in Georgia had a greater prevalence of metabolic syndrome. The greater the allostatic load, the greater the prevalence of metabolic syndrome, and females with metabolic syndrome were four times more likely to have CFS than females without metabolic syndrome.

## *Chapter 9*

### *Sleep Session*

#### **Professor Joan Shaver – The Bio-behavioural Phenomenon of Sleep/Wake**

Why do we sleep? We are not entirely certain but it seems to enable body and mind recovery, or a recharging of our batteries. We do know that sleep is important to health and that lack of restful sleep can result in daytime sleepiness, which can lead to an increased number of accidents, problems concentrating and being in a negative mood, poor performance at work or at school, and perhaps increased sickness and even weight gain.

How much sleep do we need? The amount of sleep needed varies between individuals but can be between 4.5 and 10 hours per night. Most people feel best with around 8 hours sleep per night. Some studies have shown that people who have less than 6 hours or more than 9 hours per night can have poorer health.

How do we measure sleep? Either by self-report, by asking people about their sleep, or polysomnography (PSG) which measures brainwaves, muscle tension and eye movement. Electrodes are attached to the scalp and face and connected to a recorder. Waveform patterns are scored related to stages of sleep.

When we sleep brainwaves become progressively slower and higher. There is a gradual loss of consciousness from awake to:-

- Drowsy sleep (stage 1)
- Light sleep (stage 2)
- Deep sleep (stage 3 and 4)
- Rapid eye movement (REM) sleep (stage 5)
- Back to stage 2 sleep or awake

This cycle repeats four or five times per night. During the first part of the night we experience more deep sleep, whereas later in the night there will be more REM sleep. Stage 1 sleep makes up 5-10% of our total sleep, stage 2 sleep 40-50%, stage 3 and 4 sleep 20% and REM sleep 20-25%.

During non-REM sleep, compared with being awake, heart-rate, breathing and blood pressure become slower and more regular. Muscles are more relaxed and brain blood flow decreases. But, during REM sleep, compared with non-REM sleep, heart-rate, breathing and blood pressure all become erratic. Muscles are very relaxed, effectively paralysed, brainwaves mimic the awake pattern and blood flow increases in the thalamus, primary visual, motor and sensory cortices, while it is comparatively decreased in the prefrontal and parietal associational regions.

As we get older our sleep patterns can change. We may spend more time in bed and have more time awake although the average total sleep time increases slightly after age 65. Older people tend to wake up more often, as they experience more sleep stage shifts and more fragmented sleep. Sleep may also become

lighter, ie. more drowsy, stage 1 sleep, and there may be an increase in daytime tiredness and therefore more daytime naps.

Sleep is regulated by:-

*Timing/Rhythm Component* – light/dark hormone response eg. Melatonin, ie. Circadian

*Sleep Drive Component* – Balance of neurochemicals eg. Adenosine, ie. Homeostatic

*Facilitator/Inhibitor Components* – eg. The environment and behaviours, ie. Sleep reinforcement/disturbance

Sleep difficulties can occur if there is a weak sleep drive, or excess arousal (emotional) and hyperactivation (physiological), or if there is poor synchrony with the light/dark cycle (this is why shift-workers can experience sleep problems), or negative sleep environmental conditioning. Sleep 'hygiene' and a good routine before bedtime is therefore important.

A person may have sleep difficulties due to high emotional arousal and physiological activation, which can override the drive to sleep, or hyperactive thinkers and tense individuals may have more difficulty permitting sleep drive to overtake. Treatment might include therapy to dampen down cognitive arousal and physiological activation through deep relaxation and breathing techniques as well as thought-stopping.

If there is a problem with the light/dark cycle it is simple to reset the system. The most effective way to do this is to get up at the same time every day, even at weekends, and to go to bed at the same time. Sleep restriction in the mornings will help reset the body clock.

It is also important to avoid stimulating drinks, ie. those containing caffeine or alcohol, before bedtime and to avoid strenuous exercise too close to bedtime. A bedtime routine, maybe a warm milky drink and a bath before bed can help to prepare the body for sleep.



## *Chapter 10*

### *Gender Session*

#### **Gender Aspects of CFS – Lucinda Bateman, MD**

##### *1. Both men and women with CFS face gender related challenges.*

CFS has been found to be clinically similar for men and women, with some differences in pain, function and coping styles.

Analysis of CFS gender differences in a university based referral clinic (Buchwald 1994) looked at 348 patients with CFS (288 women and 60 men). The study showed that demographic, clinical and psychosocial factors did not distinguish men from women with CFS. **Some** 51% of the women and 62% of the men were employed full or part-time and women had a higher frequency of tender/enlarged lymph nodes (60% compared with 30% of men) and Fibromyalgia symptoms (36% compared with 12% of men) and men more often had pharyngeal inflammation (42% compared with 22% of women) and lifetime prevalence of alcoholism (20% compared with 9% of women).

Dr Leonard Jason found in an analysis of socio-demographic subtypes from a community based sample that men were more likely to be working full time (78% compared with 26% of women) and less likely to be on disability benefit or unemployed. Women were more likely to have children than men, and had more children than men. Women also had more severe muscle pain (71% compared with 39% of men) and low activity levels than men. Women were more likely than men to turn to religion as a coping method, and have greater perceived stress than men.

##### *2. Clinical considerations based on gender.*

Dr Patricia Fennell's presentation was on 'Considering Gender, Sexuality and Intimacy in the Care of CFS and Fibromyalgia Patients'.

Chronic illnesses more common in women have historically been taken less seriously (e.g. Lupus, MS, PMS). The symptoms, or degree of debilitation, are often regarded as "hysterical" thus contributing to inadequate care and a delay in our understanding of the illness.

In men with CFS there is a social stigma related to having a "women's disease" which may contribute to a delay in seeking medical help, getting a proper diagnosis and appropriate care. Men and women are both guilty of gender bias against men with CFS or Fibromyalgia. Loss of work and career status, the inability to do well or compete in the workplace, the loss of business and social contacts that revolve around sports and physical activities, the inability to earn a living and support the family are all important issues (Young 2006).

Young also found that men and women have different coping styles which are not always addressed in the methodology of support groups or recognised by healthcare providers. Spouses of patients with CFS, male or female, carry a heavy burden of providing family finances, daily household and family duties, care-taking of the ill spouse, and living with the stigma and frustration of an invisible disease. They also suffer indirectly from the gender bias aimed at their ill spouse. Female spouses of male CFS patients may be less prepared to compete in the job market, may work for less money and/or take on additional work hours. Male spouses of female CFS patients may feel they lose the freedom to pursue independent interests, physical activities, travel and social events.

Couples, where one partner is ill with CFS, may need help addressing intimacy issues and sexual dysfunction, which may be related to fatigue, hormone dysregulation, medication side effects, cardiovascular or circulatory dysfunction, central or peripheral neurological factors, mood disorders, fears misconceptions.

### *3. Research considerations: heterogeneity/subset factors.*

Gender differences affect certain diagnostic tests. In the case of cardiopulmonary exercise testing, differences arose not only in the level of conditioning and the underlying disease, but also due to height, weight, BMI, age and gender (sex differences in body fat and muscle bulk, prior/current level of conditioning, attitudes about exercise etc.).

In the presentation of certain disease processes, gender differences also exist, for example, cardiovascular disease, autoimmune disease, HPA-axis and sex hormone deficiencies, mood disorders, chronic pain syndromes etc..

Consideration of gender in research is important for a number of reasons. We may discriminate against men with CFS if they are less often studied in large enough groups to achieve statistical significance, and predominantly studying women may bias our understanding of CFS. Understanding the way CFS affects men and women differently may provide important clues to pathophysiology and treatment.

## *Chapter 11*

### *Pain/Behavioural Health Session*

Dr Kenji Kato researched Chronic Widespread Pain (CWP) and its Comorbidities in Sweden. The basis of the research was that CWP, the cardinal symptom of Fibromyalgia, is prevalent and co-occurs with numerous symptom-based conditions such as chronic fatigue syndrome, joint pain, headache, irritable bowel syndrome and psychiatric disorders. Few studies have examined the comorbidities of CWP in the general population. Furthermore, little is known about the importance of familial (genetic and family environmental) factors in the etiology of co-occurrence.

Data was obtained from 44,897 individuals from the Swedish twin registry via computer-assisted telephone interviews from 1998 to 2002. The age of the respondents was greater than or equal to 42 years and the response rate was 73.2%. Screening for CWP was based on the American College of Rheumatology criteria without clinical evaluation. Measures for comorbidities were based on standard criteria when available. Odds ratios (ORs) were calculated in case-control and co-twin control designs to assess the effect of familial confounding in the associations.

Considerable co-occurrences were found in CWP cases for chronic fatigue, joint pain, depressive symptoms and irritable bowel syndrome. In co-twin control analyses ORs were no longer significant for psychiatric disorders whereas they decreased but remained significant for most other comorbidities. No changes in ORs were observed for headache.

The conclusions are that associations between CWP and most other comorbidities are mediated by unmeasured genetic and family environmental factors in the general population. The extent of mediation via familial factors is likely to be disorder-specific.

Dr Ellie Stein, from Canada, talked about behavioural interventions in ME/CFS and Fibromyalgia. She said that both ME/CFS and Fibromyalgia have high rates of psychiatric comorbidity but neither is considered to be a psychiatric disorder. No medications have been shown to cause long term, significant benefit in either disorder, therefore behavioural interventions are an obvious choice for investigation.

Correlations have been found between activity avoidance, illness attribution and illness severity but the direction of causality has not been proven. This led to the development of Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) models for ME/CFS and Fibromyalgia.

A combined CBT/exercise study (Pardaens et al. 2006) showed improved quality of life and health status but little change in exercise parameters. No study has measured the effects of CBT or exercise on symptoms other than fatigue or general function (ie. pain, sleep, infective, autonomic or cognitive symptoms are not assessed). Also, no study has measured the effect of CBT on the severely ill.

Light graded exercise has been shown to decrease pain and improve mood and quality of life in ME/CFS and Fibromyalgia patients, but CBT is not superior to other group programs (Bennett 2006) and by one year many of the effects have worn off (Redondo et al 2004). So, why don't these approaches work better? Many patients do not have dysfunctional illness beliefs (they don't attribute their illness to physical factors only nor do they show a fear of exercise). Many are already functioning at maximum activity level anyway and exercise can make some people worse.

The Stanford model for self-management of chronic illness is the most widely used model worldwide including the US, Canada, UK and Australia. The model assumes disease chronicity, patients must engage continuously in beneficial healthcare practices, patients know most about consequences of their illness and interventions, and patients and professionals must share knowledge and authority. The Stanford model includes the adoption of exercise programs, cognitive symptom management, nutritional change, energy and sleep management, use of medication and community resources, managing emotions, such as fear and depression, training in communication with healthcare professionals and the self-help manual "Living a healthy life with chronic conditions" by Lorig et al. (2000).

Following a seven week group intervention in mixed chronic conditions, followed by a two year follow-up the Stanford model has demonstrated improved self-rated health, greater participation in social/role activities, reduced disability, fatigue and health distress and also a decrease in healthcare utilisation.

New ideas to be studied include acceptance and validation. Self efficacy (perceived ability to control illness) has a positive effect on fatigue in ME/CFS. Acceptance is associated with positive physical and psychological well-being, but acceptance is also a new paradigm in the ME/CFS literature. Will acceptance of illness increase "sick role behaviour" or will it enable patients to move on?

This will depend on timely accurate diagnosis, disease specific self-management, including patient self-observation/data collection and management of sleep, activity, pain, diet, stress, emotions and environmental toxins. Patricia Fennell's four phase coping model provides a framework for the psychological work of adapting to chronic illness which takes into account an individual's place on the path to acceptance. This model encourages patients to collect data, take control of their symptoms, grieve losses and search for a new identity. Symptom-specific intervention is also important as so far research has treated all ME/CFS and Fibromyalgia patients the same, but individuals have different symptoms and respond differently to interventions. Adding a hope-based module to self-management may also improve prognosis as behaviour affects hope and hope affects behaviour.

## *Chapter 12*

### *Genetics/Proteomics/Brain Function Session*

#### **Genetics/Proteomics**

Dr Suzanne Vernon – How can we use genomics information and the tools to diagnose, treat and ultimately prevent CFS? The model used is one that interprets genomic and clinical phenotype correlations to identify significant contributors to clinical outcome. Dr Ferran Garcia-Fructuoso from Spain has conducted some interesting research on CFS and Fibromyalgia and found that the detected SNP profiles enable the most severe phenotypical forms of Fibromyalgia and CFS to be distinguished with extremely high specificity in women if samples with reliable diagnoses are used and if all the exclusions of the diagnostic criteria are respected. He has suggested that CFS could be used as an exclusion diagnosis for Fibromyalgia and has emphasised the evidence that these are two genetically distinguishable illnesses.

Proteomic research hypothesised that the clinical symptom complexes of CFS, Fibromyalgia and Gulf War Illness overlap extensively and therefore the proteomic pattern of cerebrospinal fluid proteins may be significantly different between these patients and healthy controls. The study found that the specific CFS-related proteome suggests a common pathophysiology for CFS, Fibromyalgia and Gulf War Illness.

Work by Dr Eric Aslakson showed that subspace clustering techniques can assist conventional genetic association analysis to reveal previously unknown associations. A more complete enumeration of altered pathways has demonstrated distinct and differing altered biological pathways amongst CFS subjects, further demonstrating the heterogeneity of CFS.

#### **Brain Function**

Individuals with CFS often report cognitive symptoms as the most salient and disabling symptoms significantly affecting daily function. Recently, and more commonly, the brains of CFS patients are examined with static and dynamic neuroimaging tools including MRI, SPECT, PET and fMRI.

Research in Spain and Belgium assessed 38 CFS patients using brain SPET which proved to be a useful tool in understanding CFS. A high prevalence of cortical uptake abnormalities has been found in this group of patients with CFS. The cortical uptake showed abnormalities in all the patients in the anterior temporal and cingulate cortex and in most of them in prefrontal and inferior frontal gyrus. This pattern correlates significantly with some biological markers such as elastase and even more with RNase L but does not show any relation with any other clinical parameters such as the clinical course (acute, subacute), presence of previous viral infection or the severity of the clinical symptoms. A congruent pattern has been described in basal conditions in this group of patients. The same abnormal uptake areas are present in a very high percentage of patients with variable changes in the decreased uptake values.

In another of Garcia-Quintana and Alegre-Martin's studies, 11 patients with CFS who were submitted to a stress test consisting of exercise followed by a frontal stimulation showed a brain SPET pattern with decreased post-stress uptake in frontal and anterior temporal areas.

A study by Dr Fumiharu Togo looked at information processing in CFS patients and healthy controls while controlling for the influence of a motor response component. Results showed that CFS patients have the same response accuracy as controls. After controlling for motor response time, CFS patients showed long information processing times but only in the high complexity tests. This is the first data showing impaired information processing after controlling for variables that confound the interpretation of information processing speed.

Dr Christopher Snell et al. studied brain fog or cognitive difficulties in CFS patients. For many patients these problems are exacerbated following physical activity and adversely affect their work, social, and even family lives. For such a prominent symptom of CFS research in this area has been limited.

Twenty female CFS patients and nineteen controls were given a series of reaction time tests, which included timed motor skills requiring focused or sustained attention. The CFS patients' slower reaction times across all tests provide evidence of impaired cognitive functioning compared with sedentary, but otherwise healthy, controls. In the control group, for the most part, performance improved with each test, but in the CFS patients the reaction time scores had not returned to the pre-exercise test levels even by the third test. This shows a further decrease in performance for those with CFS following a maximal exercise test.

Drs Hirohiko Kuratsune and Yasuyoshi Watanabe, from Japan, found in their brain function research into CFS, that a reduction in the density of serotonin transporters in the rostral subdivision of the anterior cingulate cortex might be related to the chronic fatigue itself, not to the non-specific symptom of pain. Furthermore, they recently found that CFS patients had a significant reduction in grey-matter volume in their bilateral prefrontal areas and that there was a significant negative correlation between the grey-matter volume of the right prefrontal cortex and the performance status of the CFS group. This suggests that CFS is not only a functional disorder, but also an organic disorder in an advanced phase.

## *Chapter 13*

### *Epidemiology Session*

#### **Epidemiology in the new century – Richard Herrell, PhD**

Epidemiology first emerged in the mid-nineteenth century as field investigations identified the causes of infectious diseases such as cholera. Even before the existence of microbes was known, John Snow observed that cholera was more common in those drinking water from pumping stations on the Thames downstream of London than in those drinking water from stations upstream. In the post World War II era, application of the same method identified smoking as the principal cause of lung cancer and risk factors for cardiovascular diseases by examining rates of these diseases in populations with and without exposures to smoking, high blood pressure, serum lipids etc. In the subsequent decades the methods of the field were applied widely to chronic diseases and injury.

By the end of the twentieth century some came to wonder if the method was simply not up to the challenge of identifying risk factors for complex, chronic diseases, caused apparently by a number of factors with small effect. In 1995, science writer Gary Taubes threw out a profound challenge to epidemiology: has it reached its limits? He cited the all-too-frequent failure of clinical trials to sustain findings from observational studies. In particular he noted the difficulties of eliminating bias from observational studies and the challenge of estimating risks with small effects as possibly insurmountable limitations of the epidemiological method. The stream of contradictory findings in the daily news had produced what Lewis Thomas called an epidemic of anxiety.

During the same decade, however, epidemiologists have also found fresh perspectives that, in fact, reflect the earliest possible health message: How and where can we intervene in the processes leading to disease, disability and death to stop the progression? A year after Taubes' report appeared, Mervyn Susser and Elizabeth Susser proposed a new paradigm for how epidemiology should direct its efforts. They proposed thinking carefully about a broad spectrum of causes, from genes to the cell to the individual to personal behaviours and social effects. The very idea of risk factor has expanded from clearly modifiable behaviours such as diet, smoking and exercise to social influences (such as neighbourhood availability of grocery stores offering fresh produce) and genes. Epidemiology has embraced these new directions in the service of identifying both the etiology of disease and the points at which intervention is possible. Both social and genetic epidemiology have blossomed as statistical methods for correlated data have become widely available. Additionally, the methods of molecular genetics have become accessible to epidemiologists as well.

The causes of diseases will continue to surprise us if we utilise the entire range of available tools and maintain focus on the entire spectrum of disease causation. Epidemiology's population and public health focus will be critical to discovery in biomedicine in the coming decades.

## *Chapter 14*

### *Viral Immune Interactions and Health Session*

#### **Stress, CFS and Viral Latency – Ronald Glaser, PhD**

Symptoms observed in CFS patients are compatible with a viral etiology. There may not be a single etiological agent for CFS; however, it is possible that CFS is associated with endogenous latent virus(es). Psychological stress has also been associated with CFS, and it has been shown that both acute and chronic stress can modulate the steady state expression of several latent Herpes viruses including Epstein Barr Virus (EBV). Researchers believe that it is useful to examine the impact of stress on the reactivation of latent Herpes viruses in the context of CFS. It is possible that a latent virus such as EBV or Human Herpes Virus 6 (HHV-6) could be involved in the etiology of at least a subset of CFS patients, especially those with acute onset illness.

Generally speaking, clinical symptoms associated with an infectious agent, for example, a virus, are due to the combination of the pathology produced by the virus and the immunopathology/sickness behaviour produced as a result of the immune response to the virus. It is possible that latent viruses, such as EBV and HHV-6 may induce immunopathology in a more subtle way, by synthesising viral protein(s) in latently infected cells or in cells in which the virus genome is only partially being expressed (incomplete replication). These proteins could induce immune dysregulation with subsequent effects on cytokine and chemokine synthesis and/or T-cell or NK cell function. Furthermore, if reactivation of the latent virus were incomplete, it could explain why it has been so difficult in obtaining consistent associations with antibody titres/patterns to a virus in CFS patients. If only a small number of viral proteins were expressed, it would not be possible to detect differences unless specific probes for these proteins were used. At the moment, we have not identified which probes to use. Furthermore, if viral reactivation was incomplete or “abortive” then virus DNA would not be synthesised making it difficult to link a virus to CFS using PCR (Polymerase Chain Reaction, where DNA is copied).

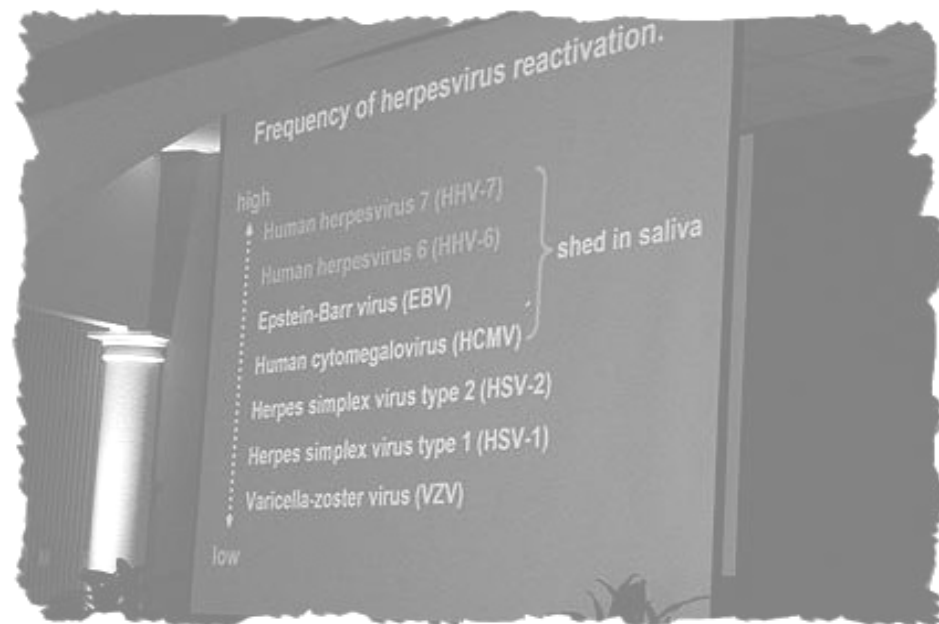
#### **Best Assays for Detecting Chronic Reactivation of HHV-6 and EBV**

Dr Dharam Ablashi and Kristin Loomis, from the HHV-6 Foundation, reviewed all the published reports on the incidence of Human Herpes Virus 6 (HHV-6) and Epstein-Barr Virus (EBV) in Chronic Fatigue Syndrome as they have produced conflicting results. Many of the studies did not utilise assays (procedure where a property of a system or object is measured) that could differentiate between active and latent virus.

The HHV-6 Foundation reviewed all studies found in medicine as well as the Journal of Chronic Fatigue Syndrome, relating to CFS or ME, that attempted to detect evidence of HHV-6 or EBV virus in patients compared with healthy subjects. They also examined the sensitivity of serum PCR in eight laboratories, using coded spiked samples of HHV-6 DNA, studied viral DNA copies in whole blood of patients compared to blood donors and studied early and late antibodies as well as several experimental assays in patients compared with controls.

The results showed that in studies where the assay was able to detect active vs. latent infection, 83% show a positive association between active virus and CFS. In studies where assays did not differentiate between active and latent virus, only 53% were positive studies. Similarly, the studies of EBV in CFS that differentiated between active and latent infection were more likely to be positive for an association. Qualitative PCR on whole blood can not differentiate between active and latent infection, and there is too little virus in the serum to make this a useful assay for chronic infection, even when highly sensitive PCR assays are utilised.

The study concluded that many past studies on the association of HHV-6 and EBV in CFS were flawed because they did not use methods that can differentiate between active and latent infection. There are now commercially available assays and highly elevated titres can be used to identify patients suspicious for active infection. Elevated PCR viral load in whole blood can also be used as a marker for active infection but larger studies are necessary to establish cut-offs. Development of newer, more sensitive and specific assays may enhance the detection of these viruses in this population.



*Slide showing the different herpes viruses and their frequency of reactivation*



*Night time scene along Seabreeze Blvd. where the Conference was held*



*Beach scene featuring a man feeding the seagulls*



*An Expert Panel answering questions from the audience*



*One of the many stands in the Exhibition Hall*



*Nancy Gordon with her 'healing dog'*



*Outstanding Male Advocate of the Year, John Herd, Jo Fisher and Rich Carson, Founder of ProHealth Inc.*



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*"Individually, we are one drop. Together, we are an ocean".*  
*Ryunosuke Satoro*



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