by Charles Lapp, M.D.

January 12-14, 2007

The 2007 meeting of the IACFS (formerly AACFS) has set new records for attendance, including more than 250 professionals and over 300 patients. An effort has been made to expand internationally, and over 21 countries were represented at this meeting!

Even before the meeting began, big changes were occurring. The IACFS Board voted to change the name of the organization to the International Association of CFS and ME in recognition of the term—ME—used by many other English-speaking nations, and thereby tendering an alternate name for this illness. Later in the week, an *ad hoc* Name Change Committee, put together by ProHealth CEO Rich Carson, also recommended using the term ME (or Mylagic Encephalopathy) in lieu of CFS. CFS will probably remain the scientific term for the illness, but it is hoped that ME will become the common designation.

Another key event at this meeting was the introduction of the new Pediatric Case Definition. A working committee of the IACFS has hammered out a proposed manner of diagnosing children and adolescents with this disorder. Research has been hampered in the past by the absence of unifying diagnostic criteria. The committee has provided a summary paper, a questionnaire for clinical use, and a summary "scoring sheet," which should help both clinicians and researchers to understand pediatric CFS/ME better.

In reviewing the papers submitted for presentation, it soon became clear that the amount and quality of research in CFS/ME has increased significantly over the past two years, and that many researchers are looking into specific aspects of the illness (such as fatigue, or pain, or sleep disruption) rather than attempting to study the syndrome as a whole.

It seems that each year a new aspect of research is introduced, and this year that aspect is "genomics and proteomics." Genomics is defined as the study of function and interactions of genetic material in the genome, while proteomics is the study of proteins made in the cell. Both

of these fields are contributing substantially to our understanding of CFS/ME and FM. As Dr. Suzanne Vernon of the CDC pointed out, it is hopeful that these studies will lead to a better understanding of the illness, perhaps a specific marker, and possibly even therapy.

Unlike previous conferences, clinical and research papers were inter-mingled this year but organized by general topic such as fatigue, sleep disorders, clinical trials, pain, epidemiology, brain function, behavioral health, pediatrics, gender aspects, and genetics/proteomics.

Fatigue Session

Seiki Tajima of Osaka, Japan, launched the meeting with a study of activity monitoring and autonomic responses in sleep. Patients wore an activity monitor (similar to a pedometer, but worn on the wrist), which was able to discriminate periods of activity, rest, and sleep during a 24-hour period. Tajima was able to identify at least 5 types of abnormal sleep patterns in persons with CFS (PWCs), including a long-sleeping type, severe insomnia, hypersomnia, and sleep phase-shifting. Autonomic (that is, R-R spectrum) analysis revealed that poor sleep may be due to a lack of parasympathetic activity during attempted sleep periods.

Nicole Porter (DePaul University, Chicago) queried PWCs and healthy individuals about their experience of fatigue. She was then able to define at least 5 different fatigue states:

- Wired fatigue—feels over-stimulated but low energy
- Brain fog fatigue—mental or cognitive impairment is associated with fatigue
- Molasses fatigue—heaviness and immobilization, unable to prolong activity
- Flu-like fatigue—weakness with flu-like symptoms
- Post-exertional fatigue—a lack of energy following minor activity

Healthy individuals experienced only one type of fatigue (typically flu-like), while PWCs experienced fatigue in diverse ways.

Elizabeth Mahoney described a CDC-sponsored study of the effect of allostatic load. One's "allostatic load" is essentially your accumulated stressors. However, the CDC used objective measures (such as heart rate, blood pressure, C-reactive protein levels, waist-to-hip ratio, lipid levels, blood sugar, insulin levels, etc.) as a measure of "load." Based on this premise, women with a high allostatic load were 5 times more likely to develop CFS/ME compared to those with low allostatic loads. This did not hold true for men, however. Mahoney also pointed out that this

study demonstrated a high prevalence of metabolic syndrome in PWCs. [Metabolic syndrome is characterized by central obesity, elevated cholesterol and triglycerides, elevated blood sugar; and the presence of metabolic syndrome frequently predicts later diabetes and cardiovascular disorders such as heart attack and stroke.]

Margaret Chicorella, both an exercise physiologist and an attorney from University of the Pacific, Stockton, CA, demonstrated how disability could be better defined using a two-part exercise test. When cardio-pulmonary exercise testing is repeated 24+ hours after the first test, oxygen consumption and the maximum achievable heart rate both decrease substantially. This is objective evidence of post-exertional malaise—a *sine qua non* of CFS/ME/FM—and could be very useful in disability determinations.

Paul Nestadt (Mt.Sinai School of Medicine, NYC) used Magnetic Resonance Spectroscopy (1H-MRS) to show that lactate is increased and N-acetyl-aspartate (NAA) is reduced in the brains of PWCs (persons with CFS/ME). Lactate levels correlated with the level of fatigue, and were not abnormal in persons with depression or anxiety. These findings are further evidence that CFS/ME is not psychiatric in origin, and that mitochondrial function and neuronal density (or metabolism) are reduced in PWCs.

Dubbo is small city in the northwest corner of New South Wales, Australia, and has been the site of several epidemiological studies concerning the clinical course of EBV mononucleosis (a DNA virus) and Q-fever (a rickettsial infection). **Toni Whistler** of the CDC described genetic findings in persons who developed PIFS, or Post-Infectious Fatigue Syndrome, which is very similar to CFS/ME. 30,000 genes were studied, and more than 40% of the pathways were found related to regulatory and metabolic pathways. Cell cycle regulation, gene regulation, and signaling were most commonly involved; and apoptotic, metabolic, and inflammatory (IL 10) pathways were prominent in the sickest patients. Whistler concluded that there is a subset of PIFS in which immune abnormalities play a significant role.

Clinical Trials

Barry Hurwitz, a colleague of Dr. Nancy Klimas at the University of Miami, presented the findings of their famous "ProCrit Study." 57 PWCs were studied for anemia and low red blood cell volume (RBCV). About 70% of the cohort actually had a low RBC volume. These were given either ProCrit (n=30) or placebo (n=10), while those with normal RBC volume were given placebo injections for 4 months. All were administered iron and dietary salt supplements also. 80% of treated subjects responded to 10,000 units per week of ProCrit, and their RBC volume increased about 26% on average. Orthostatic intolerance (by tilt table testing) improved in treated subjects, but exercise tolerance, fatigue, and other measures did not change. Thus,

ProCrit therapy might be modestly helpful for patients with orthostatic intolerance and low RBCV, but not for the general symptoms of CFS/ME.

José Montoya (Stanford University School of Medicine) described his recent valgancyclovir (Valcyte ™) studies in 12 persons with virally-induced fatigue and cognitive dysfunction. Subjects were treated with valgancyclovir for 6 months (one for 3 months only), and 9 had significant improvement in fatigue and cognition. Five of these had elevated EBV titers (VCA-IgG, EBNA, or EBV-EA), 3 had both elevated EBV and HHV-6 serologies, one had neither. None had HHV-6 elevations alone.

Comment: It is not at all clear if any of these patients had CFS/ME. We can only say that a subset of persons with Post-Infectious Viral Syndrome may respond to prolonged therapy with valgancyclovir. Dr. Montoya warned that valgancyclovir is a dangerous drug and must be used with great caution. A study of valgancyclovir specifically in persons with CFS/ME is slated to start this month, and we all anxiously await the outcome!

Martin Lerner (Wayne State University, Detroit) described a subset of patients with persistent EBV and/or cytomegalovirus (CMV), electrocardiographic changes, and symptoms of CFS/ME. In addition to having elevated IgM (or EBV-EA) titers, all 37 patients had an elevated heart rate at rest, recurrent T-wave inversions on Holter monitoring, cardiac abnormalities and/or biopsy proven cardiomyopathy. Subjects with EBV positivity were treated with high dose valcyclovir (VCV or Valtrex ™) 14mg/kg daily, and subjects with CMV positivity were treated with valgancyclovir (VGCV or Valcyte ™) for 3 to 3.5 years with improvement in fatigue, tachycardia, chest pain, syncope, flu-like symptoms, EBV titers, and cardiac wall motion. No serious adverse effects were seen.

Pain

Dan Clauw (University of Michigan, Ann Arbor) provided his usual elegant and fascinating presentation, this time on "Pain Processing and Therapy in Fibromyalgia." Clauw explained that each of us has a "volume control" for controlling the severity of pain, and that this controller is affected by both genetics and environment (or experience). Studies have shown that persons with FM (PWFs) have a normal "detection threshold" for pain, but a decreased "noxious threshold" to a variety of stimuli, including pressure, heat, noise, and electrical stimulation. Thus, PWFs sense the onset of pain the same as other individuals, but are much more sensitive to pain. This is independent of expectancy or hypervigilance.

Such findings can be demonstrated by a functional MRI scan (fMRI), which senses deoxygenated blood and thereby detects parts of the brain that are activated. Using this technique, Clauw's group has demonstrated that healthy individuals have a minimal response to a modest pain stimulus, while PWFs have a very strong response to the same modest stimulus. This proves, Clauw explains, that "when FM patients say they hurt, they really do hurt!"

Studies have also shown that pain is unrelated to co-morbid depression, but persons who catastrophize (negative thoughts, magnification of symptoms, "glass-half-empty") tend to experience more pain.

Clauw's management of pain parallels The Stepwise Approach espoused at the Hunter-Hopkins Center: education, pharmacologic therapy, aerobic exercise, alternative therapies (such as hypnotherapy, biofeedback, acupuncture, chiropracty, electrostimulation) and Cognitive Behavioral Therapy (or coaching). He reports good evidence that the following are helpful:

- Tricyclic antidepressants (amitriptyline, cyclobenzaprine)
- SNRIs (venlafaxine, duloxetine) and possibly SSRIs
- Tramadol.

There is weak evidence for using growth hormone, 5-hydroxy-tryptane, tropisetron, and SAMe; and NO evidence supports the use of NSAIDs (ibuprofen, naproxen, etc.), corticosteroids, or guiafenesin. Clauw is not a fan of opioids, narcotics, or sleep medications in the treatment of FM. Newer possible therapies for fibropain include GHB (Xyrem™), dopamine agonists (roprinolole, pramipexole), and neuromodulators.

Lastly, Clauw pointed out that there is a strong familial predisposition to fibromyalgia, with first degree relatives having 8 times the risk of developing FM. Also, Diatchenko has linked abnormalities in the COMT haplotype (which controls serotonin in the body and brain) to TMJ. This means that at least one gene codes for pain, and possibly the tendency to develop FM.

Epidemiology

Rosemary Underhill of the New Jersey CFS Association studied the prevalence of chronic fatigue and CFS in the offspring of mothers with CFS/ME. A questionnaire to members of the NJCFSA identified 108 mothers with physician-documented CFS/ME. These woman were contacted for details. There were 220 offspring. 24% of mothers had an offspring with

documented CFS/ME or chronic fatigue (CF). CFS/ME occurred in 5.5%, and 11.4% had chronic fatigue. Both sons and daughters were affected about equally, and half developed illness after age 18. 42% of the offspring with CFS/ME had already recovered, as had onethird of those with CF.

Leonard Jason (DePaul University, Chicago) calculated the economic impact of CFS/ME using both community-based and tertiary sample pools. Indirect costs (that is, loss of production) were estimated to occur in 27%, or an annual loss of $20,000 per person with CFS/ME. Direct costs (drugs, medical tests, office visits, etc.) were ascertained to be $8764 per person in the tertiary sample and $2341 in the community sample. (Patients identified from tertiary care tend to be more ill than those in the community.) Thus, the combined direct and indirect costs were $22,341 per person in the community sample and $28,674 in the tertiary sample, for an annual cost to the US economy of 19.6 to 25.2-billion dollars.

Ampligen

Dr. William Carter, CEO of Hemispherx Biopharma, reported the Ampligen experience to a crowd of interested providers before sessions began on Saturday, January 13. He stated that since the 1980's about 1000 individuals have been treated with Ampligen, using about 80,000 doses of this experimental drug. Phase III studies have been positive—showing a 16% increase in exercise ability in treated subjects—and preliminary data has been submitted to the FDA toward the New Drug Application for Ampligen. There was no speculation when this process will be complete or when Ampligen might be available to patients.

Brain Function

The current status of researching brain function in CFS/ME was reviewed by **Gudrun Lange** (University of Medicine and Dentistry of New Jersey—UMDNJ). She described some of the neurocognitive tests used to demonstrate cognitive dysfunction in CFS/ME, and pointed out that testing is much more positive in bedridden subjects (presumably sicker) and after maximal exertion (say on a bicycle or treadmill).

Radiological tools that demonstrate positive findings are MRI, CT scanning, SPECT and PET scanning (which measure cerebral blood flow), Proton Magnetic SPECT or Magnetic Resonance Spectroscopy (they measure brain metabolites such as glucose), and blood oxygen level dependent Functional MRI (or fMRI, which measures activation in areas of the brain, say to pain).

Studies so far have demonstrated that:

- PWCs perform as accurately as healthy controls, but require more regions of the brain (that is, PWCs have to work harder to get the same results);
- The key cognitive deficit in PWC's is their speed of information processing; and,
- Metabolic findings have been variable, depending on the metabolite and the group studying it.

Doctors from Barcelona, Spain, and Santiago, Chile, presented their results of SPECT scanning in PWCs compared to patients with depression. **Dr. Garcia-Quintana** showed that cerebral blood flow is decreased in the frontal lobes (only) of depressed patients, but reduced in frontal lobes and brainstem in PWCs. PWCs also have an increase of blood flow in the thalamus (a pain control center). Following exercise (or mental strain such as puzzles, short stories, or cubing numbers) the cerebral blood flow was markedly decreased in frontal, pre-frontal, anterior temporal, and cingulated regions in more than 87% of subjects studied. Increased blood levels of the enzymes elastace and RNaseL correlated with more severe loss of cerebral blood flow.

Comment: This is old news, but confirms previous studies in the US. We have known for over a decade that frontal, temporal lobe, and brainstem blood flow is reduced in PWCs, which is thought to cause problems with creativity/motivation/memory (frontal lobes), mood and memory (temporal lobes), and the sleep/fatigue/autonomic centers of the brainstem. We also knew that both exercise and mental exertion exacerbate this reduced blood flow for up to 72 hours! The new twist is that elevated elastase and RNaseL levels correlate with reduced blood flow.

Fumihara Togo (UMDNJ) presented a short but elegant paper that studied motor tasks and performance time in PWCs. Subjects would focus on a target—in this case an arrow pointing left or right—and touch one key for left, another for right. Togo demonstrated that motor performance was normal in CFS/ME, but that PWCs were slower to perform. In contrast, depressed patients had difficulty with both motor skills and speed.

A similar kind of finger-tapping study was described by Mark Van Ness, Christopher Snell, and Staci Stevens (University of the Pacific). They measured simple reaction time (the response to a simple target) and complex reaction time (response to a target hidden within other information) at rest, and then 30 minutes and 24 hours after an exercise test. They found that PWCs were a bit slower to respond than matched controls even at rest, worst 30 minutes after exercise, and still delayed 24 hours later. This held for simple or complex reaction time.

Hiro Kuratsune (Kansai University, Japan) concluded this session with a summary of what is known about brain function in CFS. We know:

- The MRI is abnormal in the majority of PWCs due to numerous T2 weighted hyperintense spots or foci, and evidence of demyelination.
- PWCs with more brain abnormalities tend to be more physically impaired.
- The volume of gray matter is reduced in proportion to reduced physical activity (that is, the brain shrinks in PWCs who are inactive!)
- Cerebral blood flow is diminished, especially in the cingulate area (controls attention, autonomic nervous system), temporal lobes (control mood, motivation), and frontal lobes (motivation, creativity, and short term memory).
- The concentration of acetyl-carnitine is reduced, particularly in the cingulate, and supplementing acetyl-carnitine may increase neurotransmitters such as GABA. glutamine, and aspartate. Acetyl-carnitine supplementation may also improve attention..
- 5-HT (serotonin) transporter binding was reduced in the rostral cingulate area in PWCs, which may help explain fatigue and pain.

Behavioral Health

Cognitive Behavioral Therapy (CBT) and Graded Exercise Therapy (GET) are commonly thought to be the only effective treatments for CFS/ME, mostly due to the influence of two meta-analyses of the treatment literature. (In actuality, these were the only two effective modalities that had been *studied extensively*, but other treatments may be helpful). Unfortunately, many practitioners concluded *errone ously* that psychiatric care and vigorous exercise were "the cure" for CFS/ME.
Dr. Ellie Stein, a psychiatrist from Calgary, Canada, eloquently addressed this in her introductory remarks.

Stein pointed out that CFS/ME and FM are chronic, heterogeneous conditions that are unlikely to respond to any single approach. It is understandable that both have high rates of psychiatric co-morbidity (such as depressed mood and anxiety), yet neither is considered a psychiatric disorder. Since no medication is known to cure CFS/ME or FM, behavioral interventions are a reasonable consideration.

The earliest CBT/GET programs were based on the false assumptions that avoidance of activity, illness severity, increased attention to symptoms, and autonomic arousal ("hyper," or hyper-excitable behavior) were causing or perpetuating symptoms, when in actuality they were the result of the illness. Of seven controlled studies using early CBT techniques, only 4 were positive and most were inconclusive or poorly done.

Five studies of graded exercise in CFS/ME showed a modest decrease in fatigue, but improvement in pain, sleep, autonomic, immune, and cognitive symptoms have *not* been shown.

It has long been suspected that persons with "pure FM" (i.e., less fatigue and cognitive dysfunction) can exert more easily, and several studies have shown temporary improvement in pain and quality of life, but many effects have worn off within a year. CBT has not been proven helpful in "pure FM."

No study has measured the effect of CBT or exercise in the severely ill.

Stein points out that CBT and GET don't work well because many patients do not have dysfunctional illness beliefs, many are already functioning at maximum activity levels, and the exercise makes some people worse! She recommends "The Stanford Model," a program for persons with chronic illness that is based on education, encouragement, and shared responsibility between patient and professional. The Stanford Model addresses low level exercise, cognitive symptom management, nutrition, energy and sleep management, the use of medication and community resources, managing emotions, and dealing with health care professionals. This program has proven success in MS, rheumatoid arthritis, and other chronic illnesses. **Dr. Pat Fennell** has also developed a proprietary chronic illness approach, based on her proposed Four Phases of Coping in CFS/ME. This model encourages patients to collect data, take control of symptoms, grieve losses, and search for a new identity.

Comment: Dr. Bruce Campbell's *CFIDS and FM Self Help Book* and his online *CFIDS and FM Self Help Course*
(both available at
www.cfidsselfhelp.org
)

are based on the Stanford Model, and highly recommended! Patricia Fennell's books are available from Barnes & Noble and other booksellers.

Stein went on to point out that self-efficacy (that is, the perceived ability to control illness) and acceptance of illness are both associated with positive physical and psychological outcomes. Therefore, CBT and GET are the most studied behavioral interventions, but results are short -ived and many do not benefit. Stein urges alternative approaches such as the Stanford Model that are more patient friendly and have a good record of success.

Professor **Fred Friedberg** (Stony Brook University) presented a short course on CFS/ME and FM to his students, and found that even a brief exposure to factual information about these illnesses led to more favorable attitudes by fourth-year medical students. Two points that students endorsed strongly were, "It is important for physicians to understand CFS," and "Patients are [NOT] to blame for their illness."

Pediatric Session

Although CFS/ME is known to occur in children and adolescents, pediatricians have been hampered by the absence of a case definition for children. The adult research definition (Fukuda, *et al*. *Annals of IM*, 1994) traditionally has been used, but children have age-specific issues and generally report different symptoms than adults. With this problem in mind, the IACFS developed the Pediatric Case Definition Working Group (Drs. Jason, Bell, DeMeirleir, Gurwitt, Jordan, Lapp, Miike, Torres-Harding and Van Hoof) to study the problem. For more than a year the committee studied various approaches to diagnosis, and developed a new definition, questionnaires, and a scoring sheet for pediatricians. This new definition combines the best aspects of the Fukuda definition with the best aspects of the Canadian Clinical Definition of ME/CFS (Carruthers, *et al*, *JCFS* (2003) 11(1):7-115), and has produced two questionnaires with queries that are age appropriate (for under 11 years old, and 11-18 years old).

To establish a diagnosis of pediatric CFS/ME the following five symptom categories must be satisfied:

- Post-exertional malaise
- Unrefreshing sleep, or a disturbance of sleep quantity or rhythm
- Myofascial, joint, abdominal, or headache pain
- Two or more neurocognitive manifestations; and

- At least one symptom from two of the following three categories:

1.autonomic manifestations

2.neuroendocrine manifestations, or

3.immune manifestations

It is hoped that this pediatric case definition will lead to more appropriate identification of children and adolescents with CFS/ME. An article on the development and use of the definition will appear in the *Journal of Chronic Fatigue Syndrome* shortly. The article, questionnaires, and scoring sheet are available online at w
ww.cfstreatment.info
, and will soon be available on
www.aacfs.org
and
www.drlapp.net
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Elke Van Hoof (Vrije Universiteit Brussel, Belgium) reported on how adolescents with CFS/ME perceive their social environment. She studied 27 Belgian adolescents (mean age 16 +/- 3 years), three-quarters of whom were female. Onset of illness was sudden in 48% of cases, and it took about 1½ years to receive a diagnosis. Only 22% were able to attend school full time, and more than half (52%) reported conflicts in school. One third (33%) got help from a teacher or classmate in order to keep up, 82% had to skip classes frequently, and 70% got failing grades. Forty percent were involved in extracurricular activities once in a while, but 48% experienced no activities outside of school. Van Hoof concluded that CFS/ME in adolescence can lead to social isolation, grades that fall below true capability, and poor attendance at school. Thus the adolescent with CFS/ME is vulnerable to a poor self image and low self efficacy.

Poster Presentations

Each year dozens of prospective papers are submitted to the scientific review committee for

consideration. Typically the best papers are presented to the entire assembly, and less solid studies are relegated to "posters" in a side room or along the walls of the auditorium. This year the quality of papers was so good that several poster authors were asked to give a brief summary of their findings to the assembly.

C. Lennartsson of the Karolinska Institute (Sweden) confirmed previous reports that low level interval training is well tolerated in CFS/ME. She was followed by **Mark Van Ness**
(University of the Pacific) whose exercise physiology group measured metabolic and immune responses to exercise. They confirmed that maximum aerobic capacity (VO2 peak) was reduced in PWCs compared to sedentary controls (24.3 ml/min/kg compared to 31.4), and the oxygen capacity at the Anaerobic Threshold was also reduced. They introduced a new measure, VO2 / workload that is also much lower in PWCs than controls (7.7 in CFS/ME compared to 8.9 in controls, where 1:320 or 1:640) of commercially available IFA assays for IgG can be used to identify patients suspected of having active infection.

Comment: Now we know that high titers of EBV or HHV-6 IgG are likely due to reactivation, and possibly amenable for antiviral therapy.

Susan Levine (private practice in NY City) and others measured IgG levels to HHV-6 and early antigen titers of EBV in persons with CFS/ME. 45% of PWCs had titers of >1:320 to EBV and 35% had titers of >1:320 to HHV-6, whereas none of 11 controls had such elevated titers. This suggests that a subset of PWCs suffer from chronic infections with EBV and/or HHV-6. Cytokines are immunologically-based chemicals that can cause viral symptoms such as fever, sore throat, swollen glands, achiness, etc. Brian Gurbaxani (CDC, Atlanta) described a simple but helpful study that demonstrated increased levels of one pro-inflammatory cytokine, Interleukin 6 (IL-6), in PWCs. His group demonstrated that increased levels of IL-6 were proportionate to CFS/ME symptom severity, but also correlated with waist-to-hip ratio (one measure of allosteric load, or "stress") and C-reactive protein (CRP), which is a marker of inflammation. This finding supports the hypothesis that an ongoing inflammatory process could be contributing to CFS symptoms.

John Chia (EV Med Research, California) reported on enterovirus infections in PWCs with GI distress. Enteroviruses (a genus of RNA viruses that includes echovirus, Coxsackie virus, and poliovirus) have been reported in CFS/ME patients by the British, but have not been explored much in the US. Chia obtained gastric biopsies on 108 PWCs with upper gastrointestinal complaints plus 12 normal healthy subjects and 9 subjects with other GI disorders. 100 of the patient biopsies revealed at least mild chronic inflammation, of which 5 demonstrated infection

with *H. pylori*. Eighty-six (86/108=80%) were positive for the VP1 (enteroviral capsid protein), while only 2/21 (10%) of controls were positive. Enteroviral RNA was detected in 5 of the 15 biopsy specimens studied (33%). Thus enteroviral infections may play a role in a subset of PWCs with upper gastrointestinal complaints.

While the evidence is not as compelling as with other infectious organisms, **Garth Nicholson** (Institute for Molecular Medicine, Calfornia) and colleagues continue to report positive PCR results for Mycoplasma species in PWCs and Gulf War Syndrome victims.

Additional Posters

Tae Park (Seoul, South Korea) reported once again on his remarkable success in treating PWCs with one gram of intravenous gamma globulin weekly for 6 months. In addition Park attends to diet, sufficient salt and water intake, regular exercise, and sleep management. He reported on 50 patients (28M, 22F), all of who were severely ill and disabled with CFS/ME. Twenty-five of the 28 males improved enough to return to work (Karnofsky Performance Score from 40 to 90; Fatigue Impact Scale from 120 to 20-40). Eighteen of 22 females remarkably improved also (KPS 40 to 80; FIS 125 to 40-50).

Comment: Four major studies using IVGG for the treatment of CFS/ME have shown variable results— two were successful, two were not. Park has abundant and continued success with his regimen, but possibly his adjunctive therapy or regular IV fluid administration contributes to some of his success?

Lastly, **Jacob Teitelbaum** (Annapolis Research Center, Maryland) provided a poster on his most recent vogue, d-ribose. Ribose is a sugar (not at all like table sugar!) that is used by the cell and specifically by the mitochondria in the production of energy. Other studies have suggested that d-ribose supplementation may improve cellular energy in heart and skeletal muscles. Teitelbaum's pilot study included 41 PWCs who took 5 grams of d-ribose thrice daily for about two weeks. Using visual analog scales, 66% of the patients reported significant improvement during the study, with an average increase of 42% in energy and 30% in well-being.

Comment: If confirmed, this is great news! I am concerned, however, over the short treatment period, which is well within the placebo effect range. Also, subjective improvement is one thing, but do any objective parameters improve? Teitelbaum states that a randomized controlled trial is underway, so perhaps we will find out soon.

Conclusions

This was an excellent and exciting meeting, perhaps the best CFS/ME conference yet. Information was so overwhelming that two weeks later I am still trying to sort it out! It is clear from the number and quality of papers submitted that CFS/ME research is beginning to thrive, and that several other nations now rival the US in this field. Particularly productive this year were Japan, Belgium, Spain, Sweden and the United Kingdom.

Two salient events during the conference were the IACFS vote to change the name to CFS/ME, and the introduction of the Pediatric Case Definition. I am sure that these recommendations will have both profound and positive consequences.

There were several themes that ran through the conference:

- Researchers are looking more at specific symptoms such as fatigue, pain, and sleep, rather than the syndrome as a whole.
- Genomics and proteomics are clearly confirming previous theories of pathophysiology, and look hopeful as a means toward a marker for the illness, clues as to causation, and a way of subtyping subjects.
- As research becomes "deeper" or more molecular, the differences between CFS/ME and FM are more distinct.
- The importance of subtyping is more recognized. At this time many researchers consider such subtypes as male/female, acute/insidious onset, severity, and whether fibromyalgia is present or not.
- The Center for Disease Control is strongly encouraging specific instruments for documenting symptoms, function, and compliance with the Fukuda Criteria, but these are not yet widely used. As a result, it is not clear what is meant when an author states that his subjects "meet international (or CDC) criteria."
- And clearly the concept of viruses or latent infections as perpetuators of CFS/ME are back in favor.

So what have I learned personally that will aid me in diagnosis and treatment?

- First of all, I will recommend testing for elastase, RNaseL, C-reactive protein, selected cytokines, and NK Cell Activity, because they are objective markers of pathophysiology and severity, and they can monitor response to therapy.
- I will recommend a test-retest approach to cardio-pulmonary exercise testing, because it

confirms for disability purposes reduced functional capacity as well as post-exertional malaise.

- I will recommend more overnight sleep studies because a majority of PWCs and PWFs have treatable sleep disorders that can be identified and monitored only by polysomnography.

- I will encourage a more multi-disciplinary approach, especially supportive counselors for those who are deeply depressed or catastrophizing.
- I will look for lipid abnormalities and evidence of metabolic syndrome in our patients, and address these problems more aggressively.
- I will recommend exploration of chronic illness models (such as Bruce Campbell's Self Help Course) as a means for group counseling and support. While graded exercise programs may be too aggressive for many patients, interval exercise and heart-rate-limited exercise programs are safe and effective therapies.
- I will test more for HHV-6a and EBV reactivation, and consider cautious administration of valgancyclovir and/or high dose valcyclovir.
- I will be recommending trials of acetyl-carnitine, d-ribose, replacement lipids (such as NTFactor ™), and antioxidants based on favorable reports presented at this conference.

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