

*by Dr. Rosamund Vallings, MB BS, ME specialist, Auckland, New Zealand*

I attended the AACFS 6th International Conference on the Chronic Fatigue Syndrome (CFS), fibromyalgia (FM) and related syndromes, held at Chantilly, Virginia from 1/31-2/2/03. The first day was a clinical conference for physicians working in the field of CFS, followed by a day and a half of research presentations.

The clinical conference opened with an introduction and overview by Charles Lapp M.D. and Leonard Jason Ph.D. Lapp ran through the history of CFS, which was described by Hammurabi as early as 2000 BC. Jason reviewed the problem of CFS and its definition, citing that 50 million Americans suffer from fatigue, of which 14 million have prolonged fatigue and 8 million have a diagnosis of chronic fatigue (not CFS). CFS fitting the research case definition probably affects 800,000 in the USA.

Epidemiologically, a major study showed that there is a predominance of females with CFS, and almost double the number of Latinos compared to American whites or Afro-Americans. There was no history of abuse in the majority of cases and in 50% of the cases there was a family history of auto-immune disease. Those with CFS were found to be more functionally impaired than those with Type-2 diabetes, congestive heart failure, MS or end-stage renal disease. Many do however show improvement over 2 years, though the majority do remain significantly impaired. Various physical and psychological scales were discussed to measure outcomes and co-morbidity, including wearing a device to produce actigraphs showing daily activity. Those with CFS particularly showed reduced activity and non-restorative sleep.

He then reviewed physical examination in CFS pointing out particularly that lymph glands and skin may be very tender. Laboratory findings in CFS were usually essentially normal, though there may be abnormal immune complexes, atypical lymphocytes, lowered IgG, small increase in alkaline phosphatase, elevations in cholesterol and small increases in ANA and thyroid antibodies. MRI studies of the brain have demonstrated high intensity T2 weighted lesions, but these do occur in other diseases and are non-diagnostic. SPECT scans to demonstrate function show decreases in cerebral blood flow with exercise, often worse 24 hours later.

There was acute onset in 85% cases, and in 72% the main precipitating factor was infection, with a small number of cases following trauma, surgery, childbirth, allergic reaction and

emotional trauma. He reviewed possible causes of CFS, including various infectious agents, immunological defects leading to T-cell activation, increases in cytokines and decreased NK-cell function, HPA-axis dysfunction with lowered cortisol levels and orthostatic intolerance. 92% of patients with CFS can become syncopal with orthostatic intolerance, and, as well as having a drop in BP, symptoms may come on after a delay of 15 minutes.

The differential diagnosis covered a very wide range of diseases, and the audience participated in discussion of the characteristic diagnostic features of other conditions such as:

- Evidence of a tick bite and presence of arthritis in Lyme disease
- Optic neuritis and ocular nerve disorders in MS
- Butterfly rash and arthritis in SLE
- Genital infection followed by arthritis (particularly in heel and lower spine) in Reiter's disease
- Skin discoloration and immediate light headedness on tilt in Addison's disease
- SSA antibodies in Sjorgren's syndrome
- Hypercalcemia with polyuria in parathyroidism
- High ferritin levels in hemochromatosis
- Gluten sensitivity and low ferritin in coeliac disease
- Raised SGOT in hepatitis etc

*Lab tests for all of the above should be performed according to the symptoms and history. Further investigation should be pursued if the ESR is elevated as that is not characteristic of CFS, when it tends to be low.*

## **Fibromyalgia**

A diagnosis of fibromyalgia (FM) is made if there is widespread pain of at least 3 months' duration coupled with tenderness in 11 of the 18 classical tender point. Gulf War Illness (GWI) tends to overlap with CFS but there are important differences, such as gastrointestinal, respiratory and skin symptoms, which are uncommon in CFS. The 1999 case definition for Multiple Chemical Sensitivity (MCS) was presented. The main symptoms are cognitive impairment, mood disorder, disequilibrium, respiratory problems, headaches, nausea and fatigue. Symptoms are reproducible with repeated exposure and tend to improve when incitants are removed. There is considerable overlap between MCS and CFS with 30% of those with MCS fulfilling the criteria for CFS.

### **Management Approach to CFS**

Lapp then presented his stepwise approach to the management of CFS. These steps include **Patient Education; Activity—**

balancing light activity with rest and increasing the level of activity slowly over time; and

#### **Nutrition—**

avoiding malnutrition, minimizing sugar, caffeine, alcohol and tobacco, keeping fats low if suffering from diarrhea and avoiding dairy products and or/gluten for 5 days to see if there is any improvement.

### **Specific Symptom Therapy:**

**Sleep Management—**Initially try melatonin, phototherapy or OTC medication, then clonazepam 0.5mg and/or doxepin 10mg (clonazepam is habituating but not addictive). Trazadone 50mg can give improvement in levels 3 - 4 sleep. Hypnotics may be needed by some patients, and flexeril can be considered in combination with any of the above.

**Central Activation—**reduced levels of dopamine and serotonin can lead to sleep disturbance, low pain threshold, loss of motivation and depressed mood. SSRIs (serotonin reuptake inhibitors) and SNIs (serotonin/ norepinephrine inhibitors, e.g. venlafaxine/ effexor) can be useful as can dopamine agonists such as wellbutrin.

**Autonomic Nervous System dysfunction—**treatment aimed at volume expansion with 2 quarts (2.5L) fluid per day with 1-2 teaspoons of salt daily. Some will benefit from fludrocortisone 0.1-0.3 mg daily. Vasoconstrictors such as ephedrine and midodrine can be useful.

**Pain Control**—presented by Ben Natelson MD:

**Stage 1:**

NSAIDS—celebrex 200mg 2x/day - often not much help.

Plaquenil—raises pain threshold, but has side effects

Tricyclics—amitriptyline 20-50mg, particularly if there is a sleep problem

Flexeril, other muscle relaxants

EffexorXR 75 -225 mg daily if depressed

**Stage 2: Anti-epileptics drugs:**

Neurontin 100mg daily, increasing to 300mg, can possibly go up to 3 gm daily

Lamotrigine 25mg daily initially rising to 100mg 3x/day

Trileptal 150mg 2x/day, rising to 600mg 2x/day

Topamax—good if there is a weight problem

**Stage 3:**

Plaquenil —6 month trial

Tizanidine—2-4mg 2x/day (very expensive)

Mexelitine—150 - 300mg daily (a local anesthetic)

Lidocaine patches maybe useful for focal pain.

Tramadol—50mg daily.

**Stage 4:**

Opiates—morphine up to 30mg 2x/day

Methadone (cheap but has long half life)

Prednisone—does not work in FM, but hydrocortisone 25mg daily is often helpful (keep in mind side-effects). A four-week trial is worthwhile.

**Treatment for Fatigue**—drugs with stimulant effects were reviewed: dexamphetamine (dexadrine), eldepryl (selegiline), cylert (pemoline), methylphenindate (ritalin), modafinil (provigil) and a new drug used for ADD called amoxetine (atomoxetine).

**Disability Evaluation** of those with CFS was then discussed by Dr. Lapp. He pointed out that in the US, primary care physicians are faced with the task of advocating for 800,000 patients with CFS and more than 2 million with FM. Up to 50% of these people are unable to work. Evaluation needs to be done by a physician familiar with CFS. Standardized psychometric and

functional testing instruments need to be used. For presentation to Social Security in the US, CFS patients must fit the 1994 Fukuda definition, with one or more specific medical signs clinically evaluated over at least 6 consecutive months (eg swollen or tender nodes, tender points etc) —and certain specific lab findings are acceptable. (eg NMH by tilt table testing, abnormal cranial MRI). Documentation of cognitive and emotional difficulties is also important. Physicians world wide should be aware of the requirements to keep good notes on relevant issues for these patients.