

The above summary of complementary approaches to Chronic Fatigue Syndrome presents an overview of the diagnostic and treatment approaches used at the Dove Clinic for this condition. The following summary offers a more scientific breakdown of these approaches and the rationale for their use.

## **CHRONIC FATIGUE SYNDROME**

### **INTRODUCTION**

Chronic fatigue syndrome is becoming increasingly common – one particular study suggests that as many as 422/100 000 people may be affected. The term essentially means ‘chronic fatigue of unknown cause’, but patients with this condition tend to have a number of other symptoms in common eg muscle pain, mood disturbance, cognitive dysfunction and sleep problems. Although in some cases there is clear evidence of a viral trigger, current medical opinion still favours the psychological model for the majority of cases i.e the idea that psychological factors play a key role in this condition, coupled with the physical deconditioning that occurs as a result of prolonged inactivity. Treatment strategies are therefore aimed at changing psychology eg via cognitive behavioural therapy and/or antidepressants etc, and at increasing activity levels by a programme of graded exercise.

There is evidence for physical/organic abnormalities in many of these patients, however, and therefore the potential for other forms of treatment exists. In a recent paper by Dr Andrew Wright MB ChB DRCOG MRCP DCH DPHom many of these abnormalities are discussed – and we have summarized them here. We have also included some relevant treatment approaches that we use at the Dove Clinic.

#### **1) IMMUNOLOGY AND TOXICOLOGY**

- In patients with CFS there is upregulation of the 2-5 synthetase RNase L antiviral pathway. This pathway is activated in all of us when we have a viral infection. It tends to cause a depletion of ATP (cellular energy stores) with resulting fatigue, and it monopolizes protein synthesis mechanisms which can interfere with other enzymatic processes in the long term eg enzymatic detoxification processes in the liver. A significant proportion of CFS patients have been shown to have an abnormal version of the RNase L enzyme which is much more biologically active and tends to cause a greater depletion of cellular energy stores. There is also evidence for a deficiency of a particular inhibitor which would normally limit the activity of this pathway.

The cause of this upregulation in CFS patients may be viral, but there is also evidence to suggest that it can occur as a result of environmental pollutants eg Methyl Tertiary Butyl Ether (MTBE) and Benzene – components of petrol fumes.

Other abnormalities seen in these patients include:

- a significant increase in Tumour Necrosis Factor  $\alpha$  (TNF $\alpha$ )
- increased apoptosis (cell death) in peripheral blood lymphocytes – possibly secondary to environmental toxins.
- unusually high levels of organochlorines
- high levels of aberrant RNA (Amplicons or Voyager RNA) - possibly due to toxin exposure and which may be associated with the development of chronic illness.
- a high incidence of multiple chemical sensitivity and allergy

**Possible tests and treatments based on these findings: (\* indicates those currently offered at the Dove Clinic)**

#### **TESTS**

- measurements of RNase L inhibitor and protein kinases may be possible – and would support a viral aetiology
- \*Natural Killer Cell activity (usually low in these patients)
- \*Rates of cellular apoptosis (expected and abnormal)
- \*Non-genomic nucleic acids (to isolate bacterial and viral genetic material) in addition to standard blood tests for viral/bacterial infection
- \*Pesticide screens and lymphocyte sensitivity tests
- \*Dark field microscopy to assess white cell activity in the live state
- \* We can also measure the energy in each of your acupuncture meridians and compare them with seasonal norms using Japanese equipment called the 'AMI'. We can then target under or overactive meridians with specific treatment programmes.

#### **TREATMENTS**

- \*To increase Natural Killer Cell activity eg pleomorphic bacterial vaccines, Biobran (MGN3)
- \*Supplementation of depleted nutrients orally or by intravenous infusion, including glutathione
- Antiviral treatments eg Ampligen
- \*Other general treatments to stimulate immune function eg infusions of high dose vitamin C, nutritional, herbal and homoeopathic treatments, intravenous ozone therapy, detoxification programmes
- TNF $\alpha$  antibodies eg Infliximab
- \*Treatment of allergy and multiple chemical sensitivity
- \*Acupuncture
- \* Anti-stress approaches based on testing for sympathetic/parasympathetic imbalance using heartrate variability tests.

There is also evidence to suggest a possible role of abnormal heat shock proteins in CFS eg due to a variety of stressors such as cold, alcohol, heavy metals, oxidants, yeast

infections and other toxins. Abnormal heat shock protein levels or function may contribute to auto-immune states, abnormal hormone and enzymatic function.

A TH2 cytokine shift has also been reported – favouring antibody production for an antigen specific immune response ( in response to toxin exposure, parasitic infection, atopy, allergy and autoimmunity). This means that there is a shift away from a TH1 response which favours the cell-mediated activity necessary to optimally remove cells infected with viruses, bacteria or protozoa, and tumour cells. Chronic stress and illness, such as in chronic sympathetic stimulation, favours TH2 cytokines. This has certain implications in relation to the effects of the specific cytokines involved, and also in relation to the subsequent efficiency of the immune system to deal with certain infections and in tumour surveillance.

- At the Dove Clinic we are able to measure cytokine levels in order to assess the activity of the TH1 and TH2 responses. This guides the choice of our treatment programmes.

## 2) ENDOCRINOLOGY

- A number of hormonal abnormalities have been seen in patients with CFS, with an additional loss of circadian rhythmicity. It seems likely that faulty input into the hypothalamus from higher centers is part of the reason for these problems, secondary to abnormal neurochemistry. Studies have shown abnormal localized brain defects which support this(eg compromised blood flow) and which also help to explain the problems with cognitive functioning and central processing of information seen in these patients.

Hormonal abnormalities commonly observed in CFS patients include the following:

- Melatonin output may be high and phase-shifted, or abnormally low – contributing to the sleep disturbances seen in these patients.
- Abnormalities in Cortisol and DHEA levels - which tend to be depressed in CFS patients. This may be due to central deregulation, or to adrenal fatigue secondary to constant biological stress.
- Abnormal thyroid function. The production of active thyroid hormones is a complicated process which depends on certain key nutrients and adequate enzymatic function. As a group, CFS patients tend to have lower thyroid activity than the normal population. In addition, some have abnormally high levels of ‘reverse T3’ which is inactive (Wilson’s Syndrome). Adequate cortisol and growth hormone levels are also important for optimal thyroid function.
- Low levels of Growth Hormone/Insulin Like Growth Factors may also be seen in these patients.
- In the chronic phase of the illness, hypothalamic function and consequently pituitary hormone output tend to be low generally

**Possible tests and treatments based on these findings: (\* indicates those currently offered at the Dove Clinic)**

**TESTS**

- \* Comprehensive hormone assays (blood, saliva, electrodermal) including reverse T3.
- \* Comprehensive assays of neurotransmitter levels and their amino acid precursors together with the presence or absence of neurotoxins – using high performance liquid chromatography on a late night urine specimen. This test can also be organized by post (simply ask us for instructions and a sample pack).

**TREATMENTS:**

- \*Nutritional supplementation, herbal and homoeopathic treatments
- \*Hormone replacement therapy.
- \* Correction of sleep disorders – allopathic, herbal, homoeopathic treatments

3) NERVOUS SYSTEM

- Sympathetic over-activity is an important component of CFS which has a number of consequences including changes in brain chemistry, endocrine and immune function, and a disturbance of lymphatic drainage. This may be central or peripheral in origin.

**Possible tests and treatments based on these findings: (\* indicates those currently offered at the Dove Clinic)**

**TESTS**

- \*Assays of neurotransmitter levels (from urine) – see previously
- \* Heart-rate variability analysis to determine the level of sympathetic overactivity

**TREATMENTS**

- \*Correction of certain neurochemical abnormalities may be possible eg by selective use of antidepressants , nutritional or other remedies
- \*Stress reduction techniques
- \*Acupuncture
- Lymphatic massage techniques

4) HYPERCOAGULABILITY

There is some evidence suggesting that the blood of many CFS patients tends to coagulate more readily than the average person, and that some patients may have a variant of the Anti Phospholipid Syndrome with the endothelial cell as the disease target. Coagulation may be activated by a variety of pathogens, and the induction of specific antibodies may result in damage to blood vessel walls – particularly affecting the microcirculation and therefore the distribution of nutrients and oxygen to cells.

**Possible tests and treatments based on these findings: (\* indicates those currently offered at the Dove Clinic)**

**TESTS**

- \*An assessment of clotting activity including predisposing factors: protein C, protein S, Factor VL, anti-phospholipid antibody and homocysteine levels.
- \*Dark field microscopy for live blood analysis (eg to show microclots and plaques, fibrin spicules etc)

## **TREATMENTS**

- \*Nutritional treatments to reduce homocysteine levels
- \*Dietary modification
- \*Intravenous ozone therapy to improve tissue oxygenation
- \*Chelation therapy
- \*Anticoagulant therapy (heparin, nutritional methods)
- \*Stimulation of immune function and treatment of contributing factors such as bacterial/yeast infections

### 5) CHRONIC INFECTIONS

In some patients, chronic ongoing infection may be playing a part in their illness. This may be viral, bacterial, yeast, parasitic etc. There is also some evidence to suggest that infection with cell wall deficient bacteria eg Mycoplasma, may be significant in these patients. There is some evidence showing that these organisms can invade tissue cells, including cells of the nervous and immune systems, and may initiate auto-immune processes as well as disrupting cellular functioning.

**Possible tests and treatments based on these findings: (\* indicates those currently offered at the Dove Clinic)**

#### **TESTS**

- \*Dark field microscopy to detect bacterial and yeast forms as well as cell wall deficient bacteria
- \*Tests specifically for the detection of Mycoplasma species
- \*Antibody levels and virology
- \*Tests for viral/bacterial infection via PCR (non-genomic nucleic acids)
- \*Comprehensive stool analysis and culture
- \*Electrodermal testing
- \*Measures of immune function eg Natural Killer Cell activity, Urinary Neurotransmitters, Cytokine assays

#### **TREATMENTS**

- \*Allopathic, herbal, homoeopathic and nutritional treatments as indicated
- \*Specific treatments to improve immune function
- \*Dietary modification

### 6) OXIDATIVE STRESS

-There is evidence to suggest that oxidative stress i.e free radical formation plays a key role in this illness. This is probably multifactorial in origin, but may particularly include the sustained increase in peroxynitrite levels (a potent free radical) due to excess cytokine production i.e from ongoing immune stimulation. Peroxynitrite also inhibits our anti-oxidant enzymes. It is suggested that this increase in oxidative stress could damage the

hypothalamus as well as causing sodium channelopathies, and uncoupling oxidative phosphorylation in mitochondria (resulting in anaerobic/glycolytic pathway dominance). Possible contributing factors include ongoing inflammation due to infection, toxicity, low anti-oxidant levels etc.

**Possible tests and treatments based on these findings: (\* indicates those currently offered at the Dove Clinic)**

**TESTS**

- \*Dark field microscopy – for evidence of oxidative damage, bacterial and yeast-like forms
- \*Anti-oxidant assays
- \*Additional key nutrient assays
- \*Electrodermal testing
- \*Cytokine assays
- \*Cellular apoptosis

**TREATMENTS**

- \*Anti-oxidant therapy
- \*Nutritional, herbal and homoeopathic treatments
- \*Treatment of infections
- \*Specific treatments to correct abnormal immune function eg to improve NKC function

**In conclusion:**

There is growing evidence for an organic basis to many of the abnormalities seen in chronic fatigue syndrome. There is invariably chronic activation of the immune system – which may result from microbial or toxin overload or both. As a result, hypercoagulability exists causing problems in both blood and lymph microcirculations. This may arise from a combination of hereditary, immune mediated and oxidative stress pathways. There is chronic sympathetic system activation, from many causes, with a subsequent high degree of oxidative stress. Multiple subtle endocrine changes are also present. Ultimately this results in a failure of homeostasis and homeodynamics.

**Treatment Summary:**

Chronic fatigue syndrome is probably multi-factorial in origin and therefore may be best addressed by a multi-factorial treatment approach. The following list suggests some of the approaches which have proved useful singly and in combination:

- Correction of nutritional deficiencies eg B vitamins, B12, magnesium and essential fatty acids. This can be done orally, by injection or intravenous infusion
- Correction of hormonal imbalances – including thyroid, adrenal, sex hormones and melatonin, and possibly growth hormone/IGF-1
- Treatment of opportunistic infections (bacterial, parasitic, yeast etc)
- Antiviral treatments
- Specific immunomodulatory therapies

- Specific anti-oxidant therapy
- Correction of sleep disorders
- Stress reduction
- Cognitive behavioural therapy
- Graded exercise programmes
- Treatment of allergy and multiple chemical sensitivity
- Dietary modification
- Specific bowel treatments
- Low dose antidepressant therapy if indicated
- Physical therapy eg acupuncture, lymphatic massage
- Oral NADH (Enada) may help some patients
- Undenatured whey proteins (may improve glutathione levels)
- Adequate salt intake – for neurally mediated hypotension
- Anticoagulation therapy
- Removal of amalgams in cases of proven mercury sensitivity, and treatment of infective foci

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