PATIENT'S INFORMATION SHEET

THE ENIGMA AND THE PARADOX OF ME

A. WHAT IS ME/CFS?:

It is a disorder initiated by a common virus infection of which (rather like influenza) several strains circulate annually in the general population giving rise to sporadic cases or to local epidemics and world-wide pandemics at 10-20 year intervals. Although clusters of infection have always been recognised in families, schools and Health Care institutions, the vast majority of cases (especially in the very young) are symptom free.[1. 2.]

B IS IT A NEW DISEASE?: [1, 2, 3, 4]

No, it is probably as old as the human race but , in communities living in temperate climates who enjoy high standards of housing and public sanitation, awareness has been raised by a striking new phenomenon of the 20th century – major epidemics of poliomyelitis (formerly a rare disease of early childhood) followed sequentially, seasonally and geographically by a parallel increase in ME/CFS (formerly considered to be an "atypical" or non paralytic form of poliomyelitis).

C IS THERE ANY PROOF THAT ME/CFS IS BECOMING MORE COMMON? [3,4,5],

Undoubtedly! – between 1934 and the decline of polio following immunisation in the early 1960's, 38 epidemics of ME/CFS were clearly recorded (in Northern parts of America, Canada, Europe and in southern areas of Africa, Australia and other well developed countries with cool/temperate climates). Since that time, outbreaks of ME/CFS have continued unabated in these areas and have also been documented from New Zealand Japan and China. No government has yet adequately funded a major demographic survey of the affected population, but individual studies estimate some 5 million cases between North America, Europe and Australasia while approximately ½ million have been reliably diagnosed in the UK (where a study of 360,351 members of the school population indicates a prevalence of 70/100,000 in pupils and 500/100,000 in staff). [6. 7.]

D THE PARADOX AND THE ENIGMA OF ME:

Why is it that ME/CFS (like poliomyelitis) becomes more rather than less common in communities with access to good housing, clean running water and the high standards of sanitation which first became universally available in the 20th century? Both disabilities are triggered by related viruses which are finely adjusted to harmless multiplication in the juvenile respiratory and intestinal tracts of humans.[7] This mutually beneficial adaptation between virus and host immune system operates to ensure life-long natural immunisation during the period between weaning from maternal antibodies in breast milk and the onset of puberty. A major hormonal disturbance (with gradual onset from 7 years of age) begins to change the host's immune T1/T2 orientation causing a breakdown in host-virus adaptation. The resulting inflammatory immune response is more severe and more chronic in

pubertal females, leading to an increase in the female to male prevalence of ME/CFS from approximate unity to 3F:1M during the childbearing years.[8] Thus, it is the reflection of a high standard of hygiene (blocking the natural circulation of these viruses via the respiratory or faecal-oral routes of infection during early childhood) rather than any genetic mutation in the viruses concerned, that leads to the paradox of "diseases of affluence" which are artificially postponed until adult life.[1]

E. WHAT ARE THE MAIN CLINICAL AND DIAGNOSTIC FEATURES OF ME/CFS? [3]

1. CLASSSIFICATION: ME/CFS is a multisystem syndrome (group of related symptoms) with variable involvement of cardiac and skeletal muscle, liver, lymphoid and endocrine organs but neurological dysfunction is essential for diagnosis. The condition is therefore classified as a neurological disease under the World Health Organisation international classification of diseases (ICD 10).

2. ONSET, PRODROMAL ILLNESS AND PROGRESSION TO CHRONICITY [3,4,9] In over 60% of cases the illness is triggered by a short respiratory/gastrointestinal infection characterised by malaise, headache, dizziness, nausea and muscle pain with or without glandular enlargement, but otherwise indistinguishable from other 'flu like or gastric upsets.

3. A more dramatic onset (following viral meningitis, myocarditis or middle ear infection, for example) is also recognised, but a trivial illness is often forgotten. In the majority of cases the infection terminates here. In others, after a variable interval, a systemic disease involving many organ systems but with major brain dysfunction, develops. This post-encephalitic process may also resolve, but other patients go on to acquire the classical symptoms of ME/CFS in which chronic low grade brain dysfunction combined with viral persistence leads to loss of bodily homoeostatis (the inability of the brain to function adequately in reception, storage and retrieval of information, thus preventing the major organs of the body from making a smooth programmed response).

3. D**IAGNOSIS:** ME/CFS has, therefore, a very distinctive and clearly recognisable symptom pattern which is present to a varying degree in all patients and which clearly differentiates it from other so-called "fatigue states", Virtually all the cardinal symptoms of this illness can be demonstrated in a GP surgery, if supplemented by a detailed history and a well kept daily record since the onset of the illness, of the hours in which the patient is able to maintain activity, (as opposed to those spent sleeping/resting), A thorough physical examination is best carried out by a doctor familiar with the patient's previous health, work or school

record and family circumstances and who is well informed about ME/CFS, particularly if similar patients have been seen in the practice. Supplementary evidence of organic disease, whether available from simple laboratory tests carried out locally (eg. to exclude other illness) or from more sophisticated and expensive research procedures,[10] is not, as yet, considered diagnostic or confirmative as it is not invariably present in such a fluctuating illness.

4. **SYMPTOMS:** The most characteristic and disabling symptoms of ME/CFS include:

i) *Episodic Post Exertional Weakness and Malaise*: These episodes are commonly provoked by physical or mental over exertion during periods of apparent well being. After a variable interval, a sense of weakness and impending collapse develops, when the patient needs to lie down. This can last for 1-7 days after the triggering event – a fact constantly overlooked in "assessment tests" or questions to ascertain the patient's exercise capacity without reference to subsequent debility. [4]

ii) *Sleep and Temperature Disturbance:* This represents a reversal of the normal daily sleep/wake and temperature rhythm, causing difficulty in keeping awake and attentive in conventional daytime hours, but with a "window" of energy somewhere within the 24 hours cycle when the subject can take advantage of recreation or study.
A 24 hour temperature chart can demonstrate inversion of normal night and daytime readings which, if taken in conjunction with a daily activity/rest record, provides a valuable guide to patients and doctors of energy fluctuations and the need to plan activities within the capacity available at any particular time.

iii) *Pain and Tactile Hypersensitivity:* Complaints of incapacitating pain in almost any part of the body are common. However, local abnormalities may not be found, since the majority of these abnormal sensations reflect central nervous system dysfunction. They may include headaches, muscle and joint pain (without inflammation) recurrent sore or "dry" throat, tender lymph glands, and extreme sensitivity to touch, vibration, light, noise, taste, smell, heat and cold.

iv) *Cardiovascular Symptoms* [11] Disturbances of the autonomic nervous system include rapid or irregular pulse rate and a tendency for the blood pressure to fall in the upright position, leading to inefficient distribution of blood among vital organs. Such irregularities of the circulation are associated with sudden faintness on standing or sitting upright and with characteristic attacks of facial pallor or flushing as well as with coldness of the limbs.

v) *Digestive Disturbances:* These include irritable bowel symptoms, constipation/diarrhoea, persistent nausea and difficulty in swallowing which, if added to distortions of taste and smell, may lead to serious appetite and nutritional disturbance.

vi) *Endocrine Dysfunction:* Owing to metabolic disturbance of the hypothalamus (the mid-brain control centre for endocrine function) patients with ME/CFS have a greater than normal risk of thyroid, pancreatic, adrenal, ovarian and other endocrine gland dysfunctions. The most common endocrine problems are associated with failure of the hypothalamic/pituitary/adrenal response to stress[12] and a tendency to insulin resistance (causing episodes of low blood sugar levels in previously healthy individuals and "brittle diabetes" in diabetic patients, already stabilised on insulin) This underlines the importance of regular meals (including breakfast!) and adequate carbohydrate intake for all sufferers.

vii) *Emotional Control*[13]: While this is notoriously variable in adolescents, patients of all ages experience sudden mood swings and additional problems often ascribed to "panic attacks" or agoraphobia when exposed to brightly lit noisy and confusing open spaces such as supermarkets and canteens. These sensations arise from incoordination of mid brain nerve networks (eg the limbic system). Disbelieving family members or colleagues must be firmly assured of the organic cause of these attacks

viii) *Cognitive and Associated Neurological Disturbance:* [14] This can be profound and may include reduced attention span, verbal and mathematical difficulties and failure of short term memory; problems with balance, fine motor control, tactile performance, impaired perception of space and shape; disturbance of vision, hearing and voice production. Many of these problems also reflect subtle changes in mid brain nerve connections rather than failure of individual sense organs.

ix) *A Prolonged Relapsing Course* [4.] This is one of the main distinguishing features of the illness in comparison with other "fatigue states" and is characterised by a series of relapses and remissions over months or years with variations in symptom patterns and recurrence of early features such as inflamed throat and glandular enlargement, in some patients.

F. UNDERSTANDING THE NATURE OF BRAIN DYSFUNCTION IN ME/CFS

Some 20 years ago, studies of the electrical activity of the brain in ME/CFS indicated abnormal slow wave patterns and unequal activity between the 2 sides of the brain in areas associated with memory, interpret-ation of speech and sound, motor control, visuospatial discrimination and other cognitive features characteristic of the illness. However, within the past 15 years, more sophisticated methods of measuring brain activity using radioactive tracers to determine metabolism and glucose utilisation (SPECT and PET scans)[10] have also disclosed fluctuating metabolic activity in the mid brain and brain stem.

This is an area which encompasses the major homoeostatic nerve centres of the body, controlling daily cycles of activity, sleep, hormone output, fluid balance, cardiovascular regulation, motor, sensory and pain control – all the vital nerve networks which maintain life! The fluctuating metabolic activity in this area readily explains the many symptoms of ME/CFS from episodic weakness to "panic attacks" - but serial SPECT scans which may indicate metabolic improvement over time, provide an impetus for correct management to encourage stabilisation of the illness in all grades of severity. Patients should therefore retain their ambitions, even if in a modified form, and never give up hope of stabilisation at some useful level of activity. To this end, they should record all symptoms (however bizarre they may seem to those who lack understanding), for this vital information could assist further research into the organic basis, of brain dysfunction in ME/CFS!

G. MEDICAL MANAGEMENT

There being, as yet, no specific medical treatment for ME/CFS, the general principles of management remain as follows:

(1) AT THE ONSET OF THE ILLNESS OR IN SEVERELY AFFECTED PATIENTS: removal from all stress and additional exposure to infection together with a sufficient period of rest and convalescence for the illness to stabilise, is recommended. Early signs of stabilisation may be recognised by a slight improvement in memory or an increase in the active versus non active energy ratio over 24 hours.

CONSERVATION OF ENERGY: This is the first and most important principle of management without which further symptomatic or experimental drug treatment cannot be expected to succeed.

a) Because most sufferers from ME/CFS are already operating at or near their maximum energy capacity while the decrease in brain metabolism following physical or mental over exertion leads to delayed recovery and relapse.

b) Because resting energy expenditure is high in ME/CFS patients[15], which means that the energy available for physical activity is being diverted to fulfil this increased requirement.

c) Because in some patients, there are additional metabolic defects in skeletal muscle leading to early lactic acidosis and increased pain and weakness, following exercise. [16]

(3) REDUCTION OF STRESS: This is best managed from the start by accepting that the illness may be long lasting and require a change in life style commensurate with the known reduction in hypothalamic/pituitary, adrenal response to stress and the resulting risk of relapse. Support from friends, families, social and financial services should be sought from an early stage but provision for recreation, holidays, and interesting hobbies is an essential strategy for stress reduction.

4) SIMPLIFICATION OF WORK. (a) For the housebound the aim must be to retain independence as far as possible by considering financial aid for domestic care and house conversion, and for home tuition or training to

facilitate paid work at home in the future. (b) For those whose illness has stabilised - it is essential to organise a gradual return to education, training or work after checking provision for mobility, modified time table, exam concessions, and part or flexitime working. (c) For those fit enough to work or study full time – a choice needs to be made of a suitable career, without undue exposure to stress, compulsary immunisations, infection, unsocial hours, difficult travel or environmental requirements. A graded career progression, without exam pressure and with facilities for, refreshment breaks and adequate holidays is desirable! NB. An initial period of voluntary work, when exercise and stress capacity can be tested, should be considered (see Dr David Bell's "All-Work-Test", below!)[17]

H. WHICH PEOPLE ARE MOST AT RISK OF ME/CFS

Exposure to infection is the main factor.[1] Occupational risks in Teaching, Health Care and paramedical professions are at least 5 times higher than in similarly stressful jobs, where employees are not exposed to infection.[7] The incidence of ME/CFS is also high in parents or carers of young children, those obliged to receive multiple immunisations for travel, as well as those engaged in sewage, refuse disposal and water industries and participants in recreational water sports. The peak age of onset in both sexes is between 30 and 40 years with a secondary peak at puberty (most marked in females). As in the case of polio, schools appear to be central to amplification and dissemination of infection to the local community.[6]

I. PROGRESS DEPENDS ON:

(a) The activity of the patient's immune system (prior contact and adaptation to the infection in childhood may ensure a trouble free host/virus relationship, while youth often appears to be an advantage). (b) The tendency of any particular strain of virus to induce serious complications (eg. cardiac). (c) The age, gender and domestic/occupational circumstances of the patient. (d) Genetic factors, (as yet undetermined) are probably less important than environmental factors such as common exposure to infection. (e) Early diagnosis and appropriate advice on management will ensure medical, domestic, educational and occupational support from the start.

J. RELAPSES MAY BE ASSOCIATED WITH [1]:

(a) Immuno suppressive events such as concurrent infection with other microbes, immunisation, steroid or cytoxic therapy. NB smoking reduces local mucosal immunity (b) Hormone disturbance, including puberty, menstruation, pregnancy but following the menopause, new onset of illness in females falls sharply. (c) Mental or physical stress arising from head injury, whiplash, surgery, malnutrition, climatic change, domestic problems, litigation, social security assessments etc.. (d) Exposure to drugs which are psychoactive or vasoactive including alcohol, anti-depressants or recreational substances and to neurotoxins, pesticides and drugs which interfere with specific neuro transmitters (eg. acetylcholine).

K. CHILDREN AND ADOLESCENTS [6]

Suffer more severely than adults from sleep and learning difficulties, weight, appetite and mood control It is essential that doctors and parents should liaise from the onset with school and other professional staff to minimise stress and contact with school infections by ensuring adequate sick leave. Home tuition, modification of class work and examination concessions must also be considered as educational deficits can be long lasting, especially in the case of young children, where they may lead to permanent language disability.

L. PROGNOSIS

This depends not only on the factors mentioned above but also on the knowledge and determination of the individual patient to use the energy available wisely. Experience gained in the rehabilitation of patients suffering from the post polio syndrome in the USA (a condition clinically similar to ME/CFS) indicate that once the principlle of energy conservation, within individual limits, has been accepted by the patients themselves, only 10% fail to stabilise.[18.]

APPENDIX[17]

Dr David Bell's "ALL WORK TEST"
"No young person with ME/CFS should be considered fit to resume school, college or work, unless they can first survive 3 hours in a Shopping Mall!"

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