INFORMATION ON ME/CFS

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ME/CFS is a complex, whole body systemic disorder and it is difficult to compile a unified reference list of the documented biomedical abnormalities, since so many medical disciplines are involved (eg. musculo-skeletal, immunological, neurological, endocrinological, gastro-intestinal, ocular, cardiovascular, respiratory etc). The reference papers themselves overlap considerably. The biomedical reference papers now number over 4,000 and some of these reference papers are listed in 92 pages of references online at **http://www.meactionuk.org.uk/SUBJECT_INDEX.htm**

The few illustrations below provide indisputable evidence of organic disease, thereby demolishing the psychiatric lobby's assertions that there is no such evidence.

The reference papers can be broadly categorised into the following sections and it is necessary to be familiar with all sections.

HISTORICAL PAPERS ON ME

These date from 1957 -- 1980 and include excellent clinical descriptions, laboratory-determined abnormalities and post-mortem findings.

GENERAL PAPERS ON ME/CFS

These papers cover more than one aspect of ME/CFS and include for example evidence of impaired oxygen delivery to muscle; evidence of delayed recovery from fatiguing exercise and documented symptoms commonly found in ME/CFS (which number over 60).

LABORATORY FINDINGS IN ME/CFS

Although there is as yet no single, specific, definitive test for ME/CFS (which is also the case in numerous other medical conditions including multiple sclerosis), nevertheless there is an entirely consistent and reproducible pattern of laboratory-determined abnormalities which have been observed and documented worldwide. Such abnormalities particularly include dysfunction of immunological, neurological, neuro-endocrinological, musculo-skeletal, cardiovascular, pulmonary and cognitive parameters.

QUALITY OF LIFE IN ME/CFS

One international ME/CFS expert writes that in his experience, ME/CFS "**is one of the most disabling diseases that I care for, far exceeding HIV disease except for the terminal stages**". Australian research describes ME/CFS patients as suffering more dysfunction than multiple sclerosis sufferers; the sickness impact profile (SIP) is more extreme than in end-stage renal disease and heart disease, and only in terminally ill cancer patients has the overall SIP score been found to reach that found in ME/CFS. American research found that the quality of life in patients with ME/CFS is significantly, particularly and uniquely disrupted, and that the illness causes marked disruption and devastation. Scandinavian research has shown that patients with "non-visible" disability suffer more stigmatisation than those with visible disability.

CHRONICITY AND SEVERITY OF ME/CFS

This section provides evidence of the natural history of severe ME/CFS, showing that the prognosis is extremely poor for the severely ill subset, with no symptom improvement (only 4% recovered) and it shows symptom patterns in long-duration ME/CFS.

PRECIPITATING FACTORS IN ME/CFS

The syndrome is known to be related to a dysfunctional stress response, and there is evidence that precipitating factors include physical trauma (specifically a breakdown in the blood-brain barrier) and critical life events. Other factors include infections; anaesthesia; immunisations and exposure to certain chemicals.

EPIDEMIOLOGY OF ME/CFS

Various papers on the epidemiology of ME/CFS reveal that considerable misinformation exists regarding the appropriate evaluation of ME/CFS (including age, gender, occupation, geographical location, length and severity of illness) but that there is increasing understanding of the prevalence, incidence, risk factors, illness patterns and prognosis of this complex multi-system disorder, and emphasis is placed on the importance of subgroups. Although ME/CFS is one of the commonest chronic neurological conditions in the UK today, no official government-sponsored statistical evaluation has yet been made, possibly due to the heterogeneity of the disorder and the lack of a concise case definition.

NEUROENDOCRINE ABNORMALITIES IN ME/CFS

This section shows evidence for and implications of the endocrine disruption found in ME/CFS, especially that associated with hypothalamic-pituitary-adrenal axis dysfunction. CT scans of the adrenal glands have revealed that both the right and left adrenal glands of some ME/CFS patients are reduced in size by 50% when compared with healthy controls.

NEUROLOGICAL ABNORMALITIES IN ME/CFS (including vertigo and seizures)

These papers show commonly found dysfunction in both the central nervous system and in the autonomic nervous system; they include papers on dysequilibrium and vertigo which are known components of severe ME/CFS, and there is evidence that seizures may occur in ME/CFS.

DEMYELINATION IN ME/CFS

Evidence of demyelination and cerebral oedema has been documented in the ME/CFS literature since 1988.

OCULAR PROBLEMS IN ME/CFS

There is evidence that such problems include intermittent jelly-like nystagmus; difficulty in accommodation / focusing / visual acuities; photosensitivity; photophobia; blurred vision; double vision; crusted eyes; dry eyes; itchiness; narrowed arterioles; retinal defects; fibrillar changes in vitreous; chorioretinal macular abnormalities and optic pallor (the latter is also observed in MS). Objective findings of the anterior segment suggest an organic aetiology.

LIVER / SPLEEN INVOLVEMENT IN ME/CFS

Published evidence shows that enlargement of the spleen and liver is not unusual. Evidence shows infiltration of the splenic sinuses by atypical lymphoid cells, with reduction in white pulp, suggesting a chronic inflammatory process.

HAIR LOSS IN ME/CFS

Hair loss in ME/CFS is documented in the literature. One author states **"It is a rare woman with CFS who has not had hair loss, usually diffuse and non-scarring**". Elsewhere, it is documented as occurring in 20% of patients.

MOUTH ULCERS IN ME/CFS

Mouth ulcers have been documented in the ME literature since 1955.

VIROLOGY IN ME/CFS

Evidence reveals the known tropism of Coxsackie B viruses for muscle, brain, heart and pancreas, all of which are documented as being target organs in ME. There is also evidence of human herpes virus 6 (HHV6) reactivation playing a role in the pathogenesis of both ME/CFS and MS. HHV6 Variant A is more common in AIDS and ME/CFS, whilst Variant B is found in MS. HHV6 used to be called human B-lymphotropic virus (HBLV); it was discovered in 1986. It is possible that reactivation of a composite viral load occurs as an epiphenomenon of an underlying immune system dysfunction, thus giving rise to the protean symptomatology.

OVERLAP OF ME/CFS WITH POST POLIO SYNDROME

Prestigious papers, for example, Annals of the New York Academy of Sciences 1995 (containing 50 papers on clinical neurology, neuroscience, electrophysiology, brain imaging, histology, virology, immunology, epidemiology, with contributors from the US, Australia, Canada, France, Sweden and the UK) point out the similarities between post-polio syndrome and ME/CFS, notably that the mechanism of the extreme fatigue (called "visceral exhaustion") -- is exactly the same in ME/CFS as in PPS.

STRESS ENHANCES SUSCEPTIBILITY TO INFECTION

There is substantial evidence that concurrent stress at the time of viral exposure leads to more severe disease. Stress is known to increase susceptibility to those diseases that are immune-related, eg. infectious disease, cancer and autoimmune disorders.

PSYCHONEUROIMMUNOLOGY

There is a vast literature (from 1884 to date) on the pathway of causation whereby stress, especially traumatic stress, affects the immune system and potentiates disease development.

CHEMICAL INJURY TO THE BLOOD BRAIN BARRIER

There is published evidence to show that one mechanism of causation is likely to be a combination of stress and chemicals, resulting in chemical trauma to the brain via a breaching of the blood brain barrier (BBB):

stress can intensify the effects of some chemicals, making them very harmful to the brain, nervous system, and liver (resulting in congested blood vessels, reduction of an important enzyme and abnormal fatty deposits), leading to cellular death, especially when chemicals are combined. The ability of chemicals to leak from one area of the brain to another holds the potential for much greater damage to occur in the entire brain.

IMMUNOLOGY IN ME/CFS

The most commonly found immune abnormalities are very low natural killer (NK) cells, with decreased cytolytic activity, and an increased CD4 - CD8 ratio; there is an increase in the CD8+ cytotoxic T cells bearing antigenic markers of activation on their cell surface; there are higher frequencies of low levels of various autoantibodies, especially anti-nuclear and anti-smooth muscle antibodies; there are low levels of circulating immune complexes; there are increased levels of IgE and decreased levels of IgG3. Low levels of IgG3 have been reported since 1986 in patients with aching muscles. Overall, these abnormalities are consistent with evidence demonstrating chronic, low-grade immune activation in ME/CFS. In 1994, an international ME/CFS expert (Dr Paul Levine of the Viral Epidemiology Branch of the National Cancer Institute, Bethesda, Maryland) stated **" the spectrum of illnesses associated with a dysregulated immune system must now include CFS"** *(ref: Clin Inf Dis 1994:18 (Suppl 1):S57-S60).* Importantly, it has been convincingly demonstrated that changes in different immune parameters correlate with particular aspects of disease symptomatology and severity.

ALLERGIES and MULTIPLE CHEMICAL SENSITIVITY (MCS) IN ME/CFS

The relationship between viral infections and onset of allergic disease is well-documented in the medical literature. With specific relationship to ME/CFS, there is overwhelming published evidence that allergies, food intolerance and multiple chemical sensitivities (MCS) are very common; an increasing sensitivity and adverse reaction to many drugs / therapeutic substances is widely believed to be virtually pathognomonic of ME/CFS. Cells cannot be attacked by the immune system unless they display on their surfaces complex glycoprotein molecules known as Class II MHC antigens; cells can be induced to do this by gamma-interferon, which is an anti-viral chemical produced by the immune system when under viral attack. Allergies in ME/CFS are thought to be the result of this mechanism, which makes the body cells susceptible to on-going attack by the immune system. Because reference to allergies is so widespread throughout the ME/CFS literature, many of these references are to be found throughout the reference papers, mostly in the sections on General ME/CFS, Immunology, and Neuroendocrinology. More and more patients are presenting with "total allergy syndrome"; this is recognised as part of ME/CFS; whilst some psychiatrists are notoriously dismissive about its existence, the literature (from highly reputable internationally acclaimed experts) clearly shows that it does exist, and that such patients do indeed develop abnormal immune parameters whilst under observation. A leading professor of clinical immunology in the UK has published papers confirming that these are patients with multiple sensitivities, and that their symptoms are not all in the mind.

ANAESTHESIA PROBLEMS IN ME/CFS

It is well-established that patients with ME/CFS and others with neuromuscular dysfunction can have problems with anaesthesia: depolarising muscle relaxants have a known risk of causing potassium release from muscle, which can lead to cardiac arrest, and it is important to avoid histamine releasers. Muscle weakness increases the risk of respiratory failure.

VASCULAR PROBLEMS IN ME/CFS

References to vascular problems in ME/CFS have been in the medical literature from 1938. Such problems include vasomotor instability; impaired blood flow in the micro-circulation consistent with inflammatory

processes; vasculopathy including Raynaud's disease; cutaneous vasculitis; vasculitis of the liver and cerebral hypoperfusion due to vasculitis.

CARDIAC PROBLEMS IN ME/CFS

Documented problems include myocarditis; chronic pericarditis; paroxysmal attacks of chest pain, with the intensity of myocardial infarction; palpitations, with sinus tachycardia being particularly troublesome; flattening and inversion of T waves; a lower stroke volume and cardiac output (indicating a defect in the higher cortical modulation of cardiovascular autonomic control). ME/CFS patients have higher heart rates and lower pulse pressure and have baseline differences from normals.

LUNG / RESPIRATORY PROBLEMS IN ME/CFS

There is evidence of shortness of breath in ME/CFS patients (due in part to fatigue of the voluntary muscles of respiration); evidence shows that ME/CFS patients have a significant decrease in vital capacity (VC). The incidence of bronchial hyper-responsiveness is remarkably high. Compared with controls, ME/CFS patients showed a significant reduction in all lung function parameters studied.

GUT DYSFUNCTION IN ME/CFS

Irritable bowel syndrome (IBS) is a widespread and common problem in ME/CFS; reference to it is to be found throughout various sections of the reference papers.

BRAIN IMAGING (NUCLEAR MEDICINE) IN ME/CFS

The literature contains objective evidence of brain impairment in the majority of patients which is compatible with a chronic viral encephalitis. Patients have a particular pattern of hypoperfusion of the brainstem. Brain perfusion impairment in ME/CFS provides objective evidence of central nervous system dysfunction.

COGNITIVE DYSFUNCTION IN ME/CFS

Neuropsychological testing reveals a pattern of cognitive impairment which is compatible with an organic brain lesion. Tests on ME/CFS patients revealed a performance which was sevenfold worse than that found in either the controls or in depressed patients. Results indicate that the memory deficit in ME/CFS is more severe than has been assumed by the CDC criteria. A pattern has emerged of brain behaviour which supports neurological compromise in ME /CFS.

PSYCHOLOGICAL PROBLEMS IN ME/CFS

There is a substantial body of literature which strongly refutes claims that patients are overly suggestible; it is quite specific that patients are not somatising, and it confirms that patients are not exhibiting "abnormal illness behaviour" and that the illness is not explained by inactivity or psychiatric disorder. Any depressive symptoms present are more likely to be a consequence rather than a cause of illness. Serious doubts are raised about the validity of the application of a psychiatric label. A conviction by patients of physical illness is demonstrated to be understandable and legitimate.

COGNITIVE BEHAVIOURAL THERAPY IN ME/CFS

Evidence shows it is at best ineffective and at worst harmful in authentic ME/CFS.

GYNAECOLOGICAL PROBLEMS IN ME/CFS

A number of gynaecological conditions have been found to occur more frequently in women with ME/CFS, for example endometriosis is reported to occur in up to 20% of women with the disorder; cystic enlargement of the ovaries may be present and can be seen on ultrasound scan. A history of ovarian cysts, including polycystic ovaries and uterine fibroids was found in one study to be more common in patients than in controls. Prostatitis is common in men with ME/CFS.

SPECIAL PROBLEMS IN CHILDREN WITH ME/CFS

It is not widely recognised that children and adolescents can suffer from ME/CFS, which has been found in children as young as five. There may be appalling problems with ignorant authorities, with children being forcibly removed from their homes and placed in the "care" of the State and the parents accused of child abuse; one consultant paediatrician who specialises in ME/CFS is on record as confirming that the number of such cases now amounts to an epidemic. The presentation in young people may differ from that in adults. Some children require tube feeding. Education may be a particular problem. There are many horrific stories of inappropriate and damaging psychiatric interventions. The Review Article by Professor Leonard Jason et al is essential reading (Chronic Fatigue Syndrome in Children and Adolescents: A Review. Karen M Jordan, Leonard Jason et al. Journal of Adolescent and Child Health 1998:22:4-18)

SIMILARITIES AND DIFFERENCES BETWEEN ME/CFS AND FIBROMYALGIA

Although there is some overlap of symptomatology in both conditions, there are significant differences between ME/CFS and FM: the WHO lists them as separate disorders in the ICD and there are important laboratory distinctions (eg. levels of somatomedin C; substance P; CBG levels; secretion of ATP; acetlycholine sensitivity; endlothelin-1 levels etc). Studies suggest that those with co-existent disorders face an additional burden of suffering and a worse outcome.

GENETIC ABNORMALITIES IN ME/CFS

There is unequivocal evidence of acquired abnormalities in numerous genes involved in energy production and with the neurological and immunological systems.

PATTERNS OF MEDICAL MISDIAGNOSIS

Misdiagnosis is very common in complex and poorly understood illness and patients are often ignored or dismissed by medical practitioners without justification. This increases their suffering. The literature abounds with evidence that patients have often been given an inappropriate label (usually by psychiatrists), and that such labels abruptly disappear when medical science and knowledge discover an underlying organic aetiology. Examples are legion, and include diabetes, hypothyroidism, pernicious anaemia, peptic ulcer, multiple sclerosis and Parkinson's disease -- in the 1940s, psychiatrists claimed that the intention tremor was due to the inner conflict of the patient who wished to masturbate but who knew it was wrong, and that the intention tremor was a manifestation of such inner conflict; it was not until the discovery of the neurotransmitters and the role of dopamine that such views were abandoned. Unfortunately, some psychiatrists seem unable learn from past experience.

A BRIEF SELECTION OF BIOMEDICAL REFERENCES ON ME/CFS

1957

An investigation into an unusual disease seen in epidemic and sporadic form in a general practice in Cumberland in 1955 and subsequent years. AL Wallis. Doctoral Thesis: University of Edinburgh, 1957. (This is an excellent and accurate description that details the varying clinical picture, the abnormal physical findings and post mortem histopathology).

1969

Disseminated Vasculomyelinopathy. Charles M Poser. Acta Neurol Scand 1969:S37:7-44. (This details postviral infectious states and subsequent development of allergies and is highly relevant in view of recent autopsy findings of severe inflammation in the dorsal horn in the case of Sophia Mirza).

1976

Benign Myalgic Encephalomyelitis or Epidemic Neuromyasthenia. AM Ramsay. Update: September 1976:539-542. (This sets out the cardinal features).

1978

An outbreak of encephalomyelitis in the Royal Free Hospital Group, London, in 1955.
Nigel Dean Compston. Postgraduate Medical Journal, November 1978:54:722-724. (This documents the clear evidence of organic involvement of the CNS).

1979

Clinical and biochemical findings in ten patients with Benign Myalgic Encephalomyelitis.
AM Ramsay; A Rundle. Postgraduate Medical Journal, December 1979:55:856-857. (This describes the dominant clinical features -- abnormal muscle fatiguability and pain; circulatory impairment and hypothalamic damage; cognitive impairment – and notes impairment of cell membrane permeability).

1981

Was it Benign Myalgic Encephalomyelitis? CS Goodwin. Lancet 1988; January 3rd: 37.
(This notes the three major features of the disease and documents abnormal physical findings).

1983

Sporadic myalgic encephalomyelitis in a rural practice. BD Keighly; EJ Bell. JRCGP June 1983:33:339-341. (This provides a good clinical summary and notes a pattern to the complexity of symptoms).

1985

Electrophysiological studies in the postviral fatigue syndrome. Goran A Jamal; Stig Hansen. JNNP 1985:48:691-694. (This documents abnormalities in muscle, including type II fibre predominance, scattered fibre necrosis; bizarre tubular structures and mitochondrial abnormalities).

1987

Myalgic Encephalomyelitis (ME) Syndrome – an analysis of the findings in 200 patients. J Campbell Murdoch. The New Zealand Family Physician 1987:14:51-54. (This describes laboratory findings, including the presence of positive smooth muscle antibodies and anti-nuclear antibodies).

1987

Phenotypic and functional deficiency of natural killer cells in patients with Chronic Fatigue Syndrome. M Caliguri, AL Komaroff et al. J Immunol 1987:139:3306-3313. (This demonstrates abnormally low numbers of NK cells).

1988

Chronic Fatigue Syndromes: relationship to chronic viral infections. AL Komaroff. Journal of Virological Methods 1988:21:3-10. (This documents unusual and abnormal findings, including hepatosplenomegaly).

1988

Allergy and the chronic fatigue syndrome. Stephen E Straus et al. J Allergy Clin Immunol 1988:81:791-795. (This documents the laboratory evidence for an allergy that is described as "substantial").

1991

Chronic Fatigue Syndrome: clinical condition associated with immune activation. AL Landay et al Lancet 1991:338:707-712. (This documents evidence for three cell surface markers and notes that CD38 and HLA DR markers remain persistently raised).

1992

A chronic illness characterised by fatigue, neurologic and immunologic disorders, and active human herpes Type 6 infection. D Buchwald, R Gallo, AL Komaroff et al. Ann Intern Med 1992:116:2:103-113. (This describes a significantly increased CD4/CD8 ratio; brain scans show punctate subcortical areas of high signal intensity consistent with oedema or demyelination in 78% of patients, suggesting patients may have a chronic, immunologically-mediated inflammatory process of the CNS).

1993

Memory deficits associated with chronic fatigue immune dysfunction syndrome. Curt Sandman et al. Biol Psych 1993:618-623. (This demonstrates that cognitive impairment is seven-fold worse than in controls and depressives and is worse than assumed by CDC criteria).

1993

Clinical presentations of chronic fatigue syndrome. AL Komaroff. Ciba Foundation Symposium 173:43-61. (This describes ME/CFS as a "terribly destructive disease"; it describes the abnormal physical examination and compares the clinical picture with that of lupus).

1996

Chronic Fatigue Syndrome: evaluation of a 30-criteria score and correlation with immune activation. Hilgers A and Frank J. JCFS 1996:2:4:35-47. (This paper notes important and consistent symptoms that are not included in the CDC 1994 case definition; these include respiratory problems, palpitations; chest pain; dizziness; dyspepsia; parasthesia; nausea and loss of hair. A correlation between the 30-criteria score and immunological parameters occurred in 472 of 505 patients).

1996

Autoantibodies to Nuclear Envelope Antigens in Chronic Fatigue Syndrome. K. Konstaninov et al J Clin Invest 1996:98:8:1888-1896. (This paper provides evidence of an autoimmune component in ME/CFS).

1997

Elevation of Bioactive Transforming Growth Factor Beta in Serum from Patients with Chronic Fatigue Syndrome. AL Bennett, AL Komaroff et al. J Clin Immunol 1997:17:2:160-166. (This paper documents the effects of TGF/beta on cells of the immune system and CNS and provides evidence that it may play a role in autoimmune and inflammatory disease).

1997

Elevated apoptotic cell population in patients with Chronic Fatigue Syndrome: the pivotal role of protein kinase RNA. A Vojdani, CW Lapp et al. J Int Med 1997:242:465-478. (This paper indicates abnormal mitotic cell division).

1997

Chronic Fatigue Syndrome: A Disorder of Central Cholinergic Transmission. A Chaudhuri, T Dinan et al. JCFS 1997:3: (1):3 -16. (This paper posits that the pathogenesis of ME/CFS involves up-regulation of post-synaptic cholinergic receptors).

1998

Relationship between SPECT scans and buspirone tests in patients with ME/CFS. Richardson J; Costa DC. JCFS 1998:4:3:23-38. (This paper provides evidence that all patients tested had hypoperfusion of the brain: 62% in the brain stem and 51% in the caudate nuclei).

1998

Neurally mediated hypotension and chronic fatigue syndrome. PC Rowe H Calkins. Am J Med 1998:105: (3A): 15S –21S. (This paper documents neuroendocrine changes and shows the link with allergy).

2000

Comparative analysis of lymphocytes in lymph nodes and peripheral blood of patients with chronic fatigue syndrome. MA Fletcher N Klimas et al. JCFS 2000:7:3:65-75. (This paper demonstrates the link with autoimmunity).

2001

Prevalence in cerebrospinal fluid of the following infectious agents in a cohort of 12 chronic fatigue syndrome patients: HHV6 & 8; chlamydia species; mycoplasma species; EBV; CMV and Coxsackievirus. Susan Levine. JCFS 2001:9: (1-2):41-51. (This paper provides hard evidence of a high yield of infectious agents in the cerebrospinal fluid of patients with ME/CFS).

2002

Symptoms occurrence in persons with chronic fatigue syndrome. LA Jason et al. Biological Psychology 2002:59:1:15-27. (This paper provides evidence of several cardiopulmonary and neurological symptoms that uniquely differentiate ME/CFS patients from controls).

2002

Cytokine response to physical activity, with particular reference to IL-6: sources, actions and clinical implications. Shepherd RJ. Crit Rev Immunol 2002:22:3:165-182. (This paper posits that exercise-induced modulations in cytokine expression may contribute to the allergies seen in ME/CFS).

2003

Abnormal impedance cardiography predicts symptom severity in Chronic Fatigue Syndrome. Peckerman A, Natelson BH et al. Am J Med Sci 2003:326:2:55-60. (This paper provides evidence of reduced cardiac output in patients with severe ME/CFS).

2004

Altered central nervous system signal during motor performance in chronic fatigue syndrome. Aiemionow V, Calabrese L et al. Clin Neurophysiol 2004:115:10:2372-2381. (This paper demonstrates altered CNS signals in controlling voluntary muscle).

2005

Urinary and plasma organic acids and amino acids in chronic fatigue syndrome. Jones MG et al. Clinica Chimica Acta: International Journal of Clinical Chemistry. Epub June 28, 2005. (This paper provides evidence for underlying inflammatory disease and for a lower threshold for muscle micro-injury).

2005

Chronic fatigue syndrome is associated with diminished intracellular perforin. Maher KJ, Klimas NG, Fletcher MA. Clin Exp Immunol 2005:142:3:505-511. (This paper provides evidence of a Tcell associated cytotoxic deficit. As perforin is important in immune surveillance and the homeostasis of the immune system, its deficiency is likely to be an important factor in the pathogenesis of ME/CFS).