

Historic Evidence of the Organicity of Myalgic Encephalomyelitis

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Note: Much of this document was previously published between April and November 2011 as three separate articles entitled “ ‘Grey’ Information about ME/CFS”, all of which are available at <https://margaretwilliams.me/> and at www.oneagleswings.me.uk/margaretwilliams/.

The “grey” literature on myalgic encephalomyelitis (ME) supports and extends the substantive published evidence-base that confirms the organicity of ME. Grey literature includes international research conference proceedings, presentations, articles and reports (including case reports and parliamentary reports) written by researchers and/or clinicians that have not been published in peer-reviewed commercial medical journals. It also includes articles written for patients’ support group magazines such as The Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) Chronicle during the 1980s and 1990s, when the CFIDS Association of America produced excellent Chronicles including “A CFIDS Primer” and “Physicians’ Forum” written by leading clinicians and researchers in the field.

The quotations variously refer to ME as “CFIDS”, “CFS” or “ME/CFS” but all are referring to authentic myalgic encephalomyelitis, not to a psychosomatic syndrome of “chronic fatigue” attributed to “aberrant illness belief” as constructed by psychiatrist Professor Sir Simon Wessely and his cohort (known as the “Wessely School”) who erroneously – and perhaps intentionally confusingly – refer to this somatoform disorder as “CFS/ME”, with their known intention of dropping the “ME” when deemed appropriate (BMJ 2003;326:595-597), thus achieving their published objective of “eradicating” ME.

Introduction

There is a substantive body of published evidence documenting the organicity of ME which cannot be in any credible doubt. ME is a multi-system organic disease; not one bodily system is unaffected, with serious dysfunction of the immunological, neurological (especially the autonomic), cardiovascular, respiratory, endocrine/ metabolic, gastrointestinal, musculoskeletal and ophthalmic systems being well-documented internationally. For a summary of such historic evidence, see Section 2 of “MAGICAL MEDICINE: HOW TO MAKE A DISEASE DISAPPEAR” pp 98 – 214 [February 2010] available at <https://margaretwilliams.me/>

This current article includes examples of the proven pathology demonstrated in ME which, to the continuing detriment of people with ME – but to the financial advantage of the Department for Work and Pensions and the health insurance industry -- is still being ignored, denied and dismissed in the UK because of the sophistry of Wessely and his co-workers who are known to have vested interests in supporting the health insurance industry to avoid legitimate claims by people with ME.

If the wealth of evidence proving the organicity of ME were to be heeded, it would destroy Sir Simon Wessely’s model of “CFS/ME” as a functional (ie. mental) disorder and would halt his continued denial of ME as an organic disorder, but such is his influence and control that this evidence has all but disappeared in the UK.

Notably, the UK NHS Policy Plus Guidance “Occupational Aspects of the Management of Chronic Fatigue Syndrome: a National Guideline” (2006/273539 / DoH Publications) with which Wessely’s colleagues (Professors Peter White, Michael Sharpe and Trudie Chalder) were involved states that the grey literature on “CFS” was not comprehensively searched in their preparation of that national guideline.

A more recent example is that in the latest edition of the standard textbook of medicine (Kumar & Clark’s Clinical Medicine: 11th edition, June 2025, published by Elsevier) ME is placed in the psychiatry section. Of concern is the fact that doctors are encouraged to read the PACE Trial, which NICE specifically does not recommend in its revised Guidelines of October 2021.

As the Countess of Mar aptly stated in 2015: “***The evidence is now so strong that ME/CFS is a serious multi-system neuro-immune disease that it becomes intellectually embarrassing for anyone to continue to consider it to be a psychosomatic disorder***” (Letter to Dr Suzanne O’Sullivan quoted in “Myalgic Encephalomyelitis: Are Wessely’s Words of Wisdom Superior to Science?” <https://margaretwilliams.me/>).

The early American CFIDS Chronicles described CFIDS (ME) as a complex illness with a constellation of symptoms that can resemble many disorders, including multiple sclerosis, AIDS-related complex (ARC), Lyme disease, fibromyalgia, post-polio syndrome and autoimmune diseases such as lupus.

Listed symptoms include profound exhaustion and malaise, especially after exercise; low grade fever; chills and night sweats; sensitivity to heat and cold; sore throat; swollen glands; muscle weakness; muscle twitching; myalgia (often a vice-like pain in muscles); neuropathic pain; sleep disturbance; headaches; chest pains; irregular heartbeat; shortness of breath; nausea; dizziness and balance problems; light-headedness; seizures; tremors; numbness or burning of the face or extremities; dryness of the mouth; rashes; allergies and sensitivities to odours, chemicals and medication; abdominal pain; diarrhoea; bladder problems; migratory arthralgias with visibly inflamed joints; transient visual scotomata (spots before the eyes); blurring of vision; eye pain; photophobia; frequent prescription changes in spectacles needed (because of difficulty in maintaining visual accommodation); hair loss; hyperacusis; forgetfulness; irritability; confusion; dyslogia (difficulty in expressing thoughts); inability to concentrate; spatial disorientation; intolerance of alcohol; emotional lability, and feeling ill all the time.

In the Summer 2008 issue of The CFIDS Chronicle, Anthony Komaroff, Professor of Medicine at Harvard, editor-in-chief of Harvard Health Publications and senior physician at Brigham and Womens' Hospital, Boston (who has published more than 230 research papers on ME/CFS) wrote an article listing **the top ten biomedical research findings in ME/CFS. These include evidence that** (1) many patients with ME/CFS have no diagnosable psychiatric disorder and that ME/CFS is not a form of depression; (2) there is a state of chronic, low-grade immune activation, with evidence of activated T cells and evidence of genes reflecting immune activation, as well as evidence of increased levels of cytokines; (3) there is substantial evidence of poorly-functioning NK cells (white blood cells that are important in fighting viral infections); (4) there is evidence of white and grey matter abnormalities in the brain; (5) there is evidence of abnormalities in brain metabolism (and evidence of dysfunction of energy metabolism in the mitochondria); (6) there is evidence of abnormalities in the neuroendocrine system, particularly in the HPA axis but also in the hypothalamic-prolactin axis and in the hypothalamic-growth hormone axis; (7) there is evidence of cognitive difficulties, especially with information processing, memory and/or attention; (8) there is evidence of abnormalities in the autonomic nervous system (including a failure to maintain blood pressure, abnormal responses of the heart rate, and unusual pooling of blood in the legs, as well as low levels of circulating blood volume); (9) there is evidence of disordered gene expression, especially in those genes that are important in energy metabolism and in genes connected to HPA axis activity, to the sympathetic nervous system and to the immune system; (10) there is evidence of frequent infection with viruses, especially herpesvirus and enteroviruses.

Laboratory abnormalities in ME/CFS include abnormal SIgA; weakly positive IgG3 (linked to gastrointestinal tract disorders); positive IgM; increased T4:T8 ratio (which always corresponds with disease severity); very low numbers of NK cells, with decreased cytolytic activity; low levels of circulating immune complexes (two-thirds of ME patients have insoluble circulating immune complexes); autoantibodies (especially antinuclear and smooth muscle); a particular HLA antigen expression; PCR evidence of abnormalities in muscle; a positive water loading test with erratic arginine-vasopressin release; a significant prolactin release in response to a single buspirone challenge; positive SPECT scans (**which show reduced blood flow through the brain stem in a particular pattern not found in any other illness or disease process apart from ME/CFS** – QJMed 1995:88:767-773); abnormal fMRI scans; abnormal EEG (80% of ME patients show prolonged jitter); a positive VP1 test; abnormal levels of mast cells; low pancreatic exocrine function; low copper response test; anomalies in trace element metabolism, especially low red blood cell levels of magnesium, zinc and chromium; low potassium levels; low peripheral oxygenation levels, with poor perfusion and pulsatilities, and increased hsCRP (a marker of inflammation).

In 2001, evidence was presented by SCM Richards et al (including psychiatrist Anthony Cleare who co-authors papers on ME/CFS with Simon Wessely) at the British Society of Rheumatologists' Conference in Edinburgh showing that 53% of ME/CFS patients were excreting in their urine significant levels of creatine and other muscle-related metabolites including choline and glycine, **indicating on-going muscle damage, as creatine has been shown to be a sensitive marker of muscle inflammation and is objective evidence of muscle pathology.**

Moreover, unlike those with other post-viral states who report that they catch opportunistic infections, people with classic ME do not succumb to every passing common cold because they have highly up-regulated interferon production, which is another distinguishing feature.

According to Peter Behan, Professor of Neurological Sciences at the University of Glasgow, as these abnormalities have been shown to occur with such regularity, if they are present and if the clinical picture is right, then a firm diagnosis of ME can be made.

The golden rule of ME experts is: if a patient improves with exercise, that person does not have ME.

This present document makes no attempt to provide a comprehensive overview of the grey literature on ME/CFS or to summarise the proceedings of international clinical and research conferences, but hopefully the illustrations provided will strengthen patients' correct perception that they suffer from a serious organic disease that is neither reversible nor curable by directive psychotherapy as asserted by the Wessely School.

People with ME/CFS and those who care for them may wish to source for themselves the presentations made at the following major conferences on ME/CFS; these include the US NIAID (National Institute of Allergy and Infectious Diseases) Symposium held at the University of Pittsburgh in September 1988; the Rhode Island Symposium in 1988; the Rome Symposium in 1988; the San Francisco conference in April 1989; the British Post-Graduate Medical Federation Conference in London in June 1989; the Los Angeles International Conference in February 1990; the First World Symposium held in 1990 at Cambridge University, UK; the Charlotte Research Conference in November 1990; the Canadian Workshop at the University of British Columbia, Vancouver, in May 1991; the Dublin International Symposium in May 1994 (held under the auspices of The World Federation of Neurology); the First World Congress (also under the auspices of The World Federation of Neurology) in Brussels in 1995; the Second World Congress in Brussels in September 1999; the Bloomington Conference in Minnesota in October 2001, and the International Clinical and Scientific Meetings presented by the Alison Hunter Memorial Foundation in Australia, especially the Third International Meeting in Sydney in December 2001; the biennial International Research and Clinical Conferences hosted by the American Association of CFS (AACFS, now the IACFS / International Association of CFS), including the Albany, New York, conference in October 1992; the Fort Lauderdale, Florida, conference in October 1994; the San Francisco conference in October 1996; the Boston, Massachusetts, conference in October 1998; the Seattle conference in January 2001; the Chantilly, Virginia (Washington D.C.) conference in January – February 2003; the Madison, Wisconsin, conference in October 2004, the Professional Research Conference in Fort Lauderdale in January 2007, and the numerous Scientific Workshops such as the one co-sponsored by the US National Institutes of Health in June 2003 on neuro-immune mechanisms in ME/CFS and the ME Research UK (MERUK, formerly MERGE) workshops (including the Royal Society of Edinburgh funded Workshop in 2003, the MERUK Colloquium in July 2006 and the MERUK International Research Conference on 25th May 2007 at Edinburgh), plus the 17 annual international biomedical research conferences in London hosted by Invest in ME Research, the aim of all these conferences and colloquia being to facilitate links between research scientists and clinicians working towards the common goal of understanding the biomedical basis of ME/CFS.

The following illustrations present a picture of authentic ME that is nothing like the Wessely School's "behavioural" model of "CFS/ME" which ignores the key symptoms of ME and is based on "fatigue" and which many people believe is a travesty of medical science.

Illustrations

1956: Dr ED Acheson, later to become Chief Medical Officer for England and Wales, coined the term "benign myalgic encephalomyelitis", stating: ***"In nearly every patient there are signs of disease of the central nervous system"*** (A New Clinical Entity? Editorial: Lancet: 26th May 1956).

(**Note:** the word "benign" was included to indicate that although the disease was serious, it was not invariably fatal, but the word "benign" has been used by Wessely apparently to denote that ME is not a serious disorder).

1957: ***"There were changes in the blood picture in 30% of cases. There was objective evidence of CNS involvement...with subjective neurological phenomena in over 60% of cases"*** (AL Wallis. Doctoral Thesis University of Edinburgh 1957). **Wallis lists the following neurological signs and symptoms: parasthesiae; hyperasthesiae; impairment of taste and smell; vertigo; blurred vision; loss of concentration; poor recent memory; impairment of co-ordination and unsteadiness; general weakness (a frequent complaint: walking, lifting and carrying were all limited); inversion of sleep rhythm (ie. sleep reversal); pupils frequently sluggish in reaction to light and accommodation; ptosis of eyelid; hyperacusis (commonly found); nystagmus; neuralgic pain was commonly complained of; alteration in speech; nominal aphasia; ataxia; Romberg commonly positive; observable tremor; impaired judgment of distance; a variable reflex state was found, being brisk in a large number of cases, with knee and ankle clonus.**

Wallis provides evidence of objective sensory and autonomic disturbance, as well as details of *post-mortem* histopathology, which is particularly interesting given the long history of vasculopathy and impaired blood flow

in ME. (**Note:** Wallis' description of ME is set out in detail in "Vade MEcum" [28th June 2005] available at <https://margaretwilliams.me/>).

1977: *"Objective manifestation of the disease can still be present over thirty years after the initial illness"* (AM Ramsay, EG Dowsett et al: BMJ 21st May 1977:1350).

1978: *"It became clear early on that there was organic involvement of the central nervous system. Bladder dysfunction occurred in more than 25% of all patients. Objective evidence of brain stem and spinal cord involvement was observed"* (ND Compston: Postgraduate Medical Journal 1978:54:722-724).

1981: The Lancet published a letter from Professor CS Goodwin about necessary criteria for a diagnosis of ME: *"Firstly, symptoms and signs in relation to muscles, such as recurrent episodes of profound weakness and exhaustion, easy fatigability, and marked muscle tenderness. Secondly, neurological symptoms or signs – pyramidal or cranial nerve lesions, especially affecting the eyes; or weakness of peripheral muscles as demonstrated by the voluntary muscle test; or some loss of peripheral sensation; or involvement of the autonomic nervous system (orthostatic tachycardia, abnormal coldness of the extremities, episodes of sweating or pallor, constipation and bladder disturbances. Thirdly, biochemical abnormalities, such as raised urinary creatine, low serum pyruvate, or raised serum myoglobin, or an abnormal electrophoresis pattern with raised IgM"* (Lancet, 3rd January 1981:3:37).

1983: *"ME (is) a distressing and often prolonged illness...As the study progressed, a pattern to the complexity of the symptoms developed (which included) malaise, exhaustion on physical or mental effort, chest pain, palpitations, tachycardia, polyarthralgia, muscle pains, back pain, true vertigo, dizziness, tinnitus, nausea, diarrhoea, abdominal cramps, epigastric pain, headaches, paresthesiae and dysuria. The group described here are patients who have had miserable illnesses"* (BD Keighley EJ Bell JRCGP June 1983:339-341)

1985: Dr RW Gorringer from New Zealand published "Diagnostic Criteria and Tests for ME" in October 1985, which provided a comprehensive and useful diagnostic tool; Gorringer warned that *"the commonest mistake doctors make is failing to take a wide enough view and cover an adequate systems review"*. He noted the classic symptoms of ME including prominent but intermittent chest pain (severe enough for hospital admission); sore muscles of the shoulders, neck and back; muscles that become shaky and tremulous; frequency of micturition; irritable bowel (colicky abdominal pain and loose bowels); moist chest; cough; palpitations; jerkiness of limbs; difficulty in co-ordination; paresthesiae; shooting pains up nerves; blurred vision; burning pain behind the eyes; oesophageal spasm; food allergies; sensitivity to light; intermittent swollen glands and sore throat; dizziness and nausea. Gorringer noted evidence of malabsorption and hypoglycaemia (in ME/CFS patients, blood sugar is known to be under poor control); he pointed out that on TFT (thyroid function test), TSH was often normal but that T3 may be low, with subclinical hypothyroidism. He also noted abnormal immunoglobulins, particularly IgA (often low) and IgM (which goes up in a relapse but may sometimes be depleted and become markedly decreased), and abnormal CICs (circulating immune complexes), with low C3 and C4 (the modified immunoglobulins do not make proper complexes with allergens taken in, resulting in (insoluble) circulating immune complexes in the central nervous system, in the joints and in the kidneys, which can be a very hazardous state).

1987: in his Medical Address at the AGM of the ME Association on 25th April 1987, James Mowbray, Professor of Immunopathology, St Mary's Hospital Medical School, London, said: *"If someone has IgM antibodies they have either been recently infected or they are still infected....We developed a technique using a specialised antibody...which detects a protein in enteroviruses which is the same in all 72 enteroviruses (and) we can use that antibody to look for the virus protein in the blood. Doing that, we have been able to find a very large fraction of the ME patients have got an enterovirus antigen....Just because you find virus proteins in the blood, does that mean they are infected? Yes, it does....The virus is present in the intestine. It is also shown to be present in the muscle....The virus is being made and is switching off host genes stopping the cells' own energy*

production. If you now exercise, you rapidly run out of energy in the muscle and that has been shown by sophisticated techniques....Whilst (the virus) is there, it severely limits the ability of the muscle to work....The thing that seems to make it worse is exhausting the muscle.... When you have got the disease it is a good basis for saying do not use up all the muscle energy, do not get to that stage. It may lead to more virus affecting that muscle....It is clear that it is not only exhaustion in the muscle but also in the brain....Either muscle or brain overdoing it is the same.... and we have now got some good scientific background”.

1987: At the US CFS Society conference held on 4th-7th November 1987, Infectious Diseases specialist Dr Mark Loveless from the University of Oregon said that **the musculoskeletal, neurological and vestibular systems were involved, and that there are cardiovascular, gastrointestinal and immunological abnormalities**. At the same conference, Dr Alfred Johnson said that 97% of (ME/CFS) patients have allergies and that allergic patients have high helper (T4) cells and low suppressor (T8) cells, causing over-reactivity. **Dr Paul Cheney confirmed that the T4:T8 ratio is elevated in two-thirds of cases, and that this is considered a more reliable marker of the illness than other markers. He said there are “impressive abnormalities” in mitogen stimulus status** (an immune function test) and that symptoms are caused by a hyper-immune response. **He noted that MRI scans showed characteristic brain lesions in 77% of patients tested (88 of 114 patients) as determined by two independent neurologists.**

1988: Professor James Mowbray’s team at St Mary’s Hospital, London, began to offer a test for the detection of enteroviral protein in ME patients. VP1 stands for Viral Protein 1, described in the ME Association’s magazine in Autumn 1988 as being: *“one of four proteins forming together the viral capsid which surrounds the viral genetic material. There is a particular portion of the VP1 protein which is present in all 72 different enteroviruses”*. The ME Association offered the test to its members for an administration fee of £3. The following year, at the Clinical Session of the 1989 AGM of the ME Association, Dr Byron Hyde from Canada referred to the VP1 test, confirming what Professor Mowbray himself had said: **ME patients with a positive VP1 test become chronic, whilst those with a negative VP1 test recover. Despite this, the VP1 test was dismissed by psychiatrist Simon Wessely as “unsuitable for routine clinical use”** [Lancet 1989:1:1028-9] and it is no longer available in the UK.

1988: An article by Elsie Brody (Occupational Health, 1988; 446-447) listed key symptoms of ME, including severe headaches, neck pain, pain in back and limbs, pins and needles in limbs, vertigo, severe sweating, impaired memory and difficulty with words, panic attacks (now known to be due to hyperadrenergic orthostatic intolerance), tachycardia, extreme fatigue, disturbed sleep, muscle weakness and tenderness, diplopia, photophobia and chest pain. Mrs Brody advised that: *“As OH professionals, it is our duty to recognise the disease early (and) educate management on recognising ME”*.

1988: The ME Association’s magazine “Perspectives” carried an article on “Viruses and ME” by consultant microbiologist Dr Betty Dowsett, who wrote: *“Many viruses (including enteroviruses) can enter and alter the function of the immune cells specially designed to destroy them. It is important to recognise that these immune abnormalities are secondary to the virus infection....The mopping up of free viruses in the bloodstream can be counter-productive if excess antibody is produced. The insoluble ‘immune complexes’ that result can be trapped in the blood vessels and tissues and...maintain infection in the body....The chemical composition of a virus may mimic that of a normal body component (such as brain or muscle protein) whereupon the immune attack is misdirected against the host while the virus disappears unnoticed. Cardiac and other complications in ME are an example of such an anomaly”*.

1988: At a meeting on ME held at The Royal Free Hospital on 16th May 1988, Professor Tim Peters from Northwick Park Hospital said his team had found abnormalities of Type II muscle fibres (anaerobic) in ME patients, which were atrophied, with hypertrophy of Type I muscle fibres; **he had measured total RNA in muscle cells and found it to be significantly reduced in ME patients (if there is a decline in RNA, there is a decline in the ability to make muscle protein – infusion of tag-leucine showed overall metabolism is clearly reduced and the rate at which muscle is being formed is reduced).**

1989: Professor Peters (then Professor of Clinical Biochemistry and Consultant Chemical Pathologist at Kings College Hospital, London) wrote on page 24 of the magazine InterAction No: 3 of the charity ME Action, now AfME: ***“Exciting studies have recently been reported of persistent viral RNA in biopsies from patients with ME....Based on these observations we have started to investigate muscle protein synthesis; that is, the ability of muscle to repair itself...in patients with ME. Measurements of muscle RNA, the machinery for protein synthesis, showed consistently reduced amounts in their biopsies. Studies of whole body and, specifically, thigh muscle protein synthesis rate in these patients show reduced values and thus a pattern is beginning to emerge of persistent viral infection, and possibly re-infection, interfering with the machinery for making tissue protein and thus impairing protein synthesis”.*** Discussing the view of those who claim that changes in mitochondrial function and impaired muscle synthesis are merely secondary events due to lack of use of the muscles, **Professor Peters continued: “It is hard to see how (this) can explain the persistence of enteroviral RNA in muscle fibres....immobility leads to a selective loss of Type I fibres, a feature not seen in patients with ME”.**

The same issue of InterAction reported on page 22 **the neurological abnormalities found by Carolyn Warner and her team from Buffalo, NY (elevated IgG synthesis, elevated CSF cell count, prolonged visual evoked response latency, abnormal EEG and MRI lesions, and neuromuscular abnormalities including over 20% polyphasic motor units on quantitative EMG, inflammatory infiltrates and Type II fibre atrophy, these being reported in Neurology 1989;39:Suppl 1: 420).** Commenting on these abnormalities, **Dr Goran Jamal, Consultant in Clinical Neurophysiology at The Institute of Neurological Sciences, Glasgow, affirmed that those results are consistent with disturbed immune function and persistent infection, and that it proves once again that one can find neurological abnormalities if one looks.**

Still in the same issue of InterAction, Dr Jamal himself wrote on page 26 about muscle fatigue in ME: ***“In recent years a lot of evidence has been accumulating to suggest that the fatigue in ME is organic in nature....Our findings clearly showed evidence of disturbance of transmission of electrical impulses along muscle fibres. This study... provided one of the first and strongest indications for the organicity of the syndrome. This work has been reproduced again by our group and elsewhere. In addition we have looked at other groups of patients with various psychiatric illnesses using the same technique of single fibre electromyography, and these produced absolutely normal findings....Examination of individual muscle fibres under electron microscopes...showed gross abnormalities of the structures involved in providing energy for the muscle fibres....NMR (nuclear magnetic resonance) showed evidence of disturbed muscle metabolism....Strong evidence of the presence of viral particles in the muscles of ME patients has also recently been shown....Any assumptions that the fatigue in patients with ME is entirely ‘mental’ or ‘psychogenic’ is not only without any foundation but also ignores all this solid scientific data”.***

1989: Dr Paul Cheney from the US presented his findings at the San Francisco CFS Conference on 15th April 1989; **70% of ME/CFS patients tested had depressed levels of salivary IgA (SIgA), and ME/CFS patients with low SIgA levels tended to have high levels of insoluble circulating immune complexes. Microscopic analysis of tissues showed lymphocytic vasculitis (lymphoid infiltrates in the blood vessel wall) in 75% of patients tested.**

1989: In a talk given on 15th May 1989, Peter Behan (Professor of Neurological Sciences at the University of Glasgow) said that ME is a viral infection of the gut with gross exhaustion and tachycardia accompanied by malaise. He said the real tragedy of ME is the far-reaching effects on the medical profession of two not-very-talented psychiatrists in 1977 (McEvedy and Beard), one of whom had only just qualified. **Behan stressed the importance of separating psychiatric fatigue from ME fatigue.** He explained that the brain produces Interleukin 1 (IL-1) as a result of the cell being stimulated by a virus, and IL-1 will cause the liver to be abnormal; it will affect muscle and nerve cells, and it is found in extreme fatigue. He said that **in the majority of true ME cases, IL-1 levels are extremely high.**

1989: In the summer issue of the ME Association's magazine, Dr David Smith wrote about slow-onset ME: *"I am afraid that there is probably less chance of a spontaneous cure, and in that disease undoubtedly there is a natural progression of symptomatology....I do believe that the slow onset.. persistent enterovirus infection is ME"*. In "A Letter from our President" in the winter issue of the ME Associations' magazine, Dr Melvin Ramsay wrote: *"The onset of the disease may be sudden or gradual....The crucial difference between ME and other forms of postviral fatigue syndrome lies in the striking variability of the symptoms, not only in the course of a day but often within an hour. This variability and intensity of symptoms is not found in postviral fatigue states"*.

1990: On 17th March 1990 Professor Peter Behan from Glasgow made a presentation to the Mid-Anglia branch of the ME Association in Cambridge. He began by giving an over-view of the historical perspective and went on to discuss the cardinal symptoms of ME, these being (1) onset precipitated by a viral infection; (2) local and generalised fatigue arising from the brain as in multiple sclerosis; (3) post-exercise myalgia, especially in the shoulder girdle, back, neck and left side of the chest; (4) mental changes, including poor control of emotions, poor task performance and cognitive disturbances; (5) sleep disturbance; (6) **cardiac disturbances (a significant number have cardiac symptoms) and (7) vestibular disturbance, with dysequilibrium and sometimes true vertigo**. He discussed the hypothalamic dysfunction, noting that **50% of ME patients cannot produce steroids in response to stimulus. He presented objective evidence of Type II muscle fibre atrophy on histological section and evidence of mitochondrial damage, and showed identification of enteroviral RNA in muscle.**

1990: On 10th- 12th April 1990 the First World Symposium on ME/CFS was held at the University of Cambridge. Speakers presented evidence on acute, latent, persistent and reactive virus/host interaction; on cytopathological studies; on electron microscopy studies; on immunological abnormalities, genetics and autoimmunity; on interferons and their role in virus infections; on muscle studies of abnormal metabolic function; on cardiac disease in ME/CFS; on lesions in the brain and on paediatric ME/CFS. **The predominant view was of a persistent or chronic viral infection which either gave rise to, or was the result of, a continuing abnormal immune response and abnormalities of the muscle and central nervous system. Evidence was presented of an infective vasculitis in ME/CFS.** The Symposium brought together leading international researchers to review all aspects of ME/CFS. The proceedings were subsequently published as the 724-page seminal textbook on ME/CFS (The Clinical and Scientific Basis of Myalgic Encephalomyelitis Chronic Fatigue Syndrome, edited by Drs Byron Hyde, Jay Goldstein and Jay Levy; The Nightingale Research Foundation, Ottawa, 1992). **The conclusion of the Symposium was plain: ME/CFS is a true organic disease, with abundant evidence of its organicity.**

1990: In September 1990 the CFIDS Association of America produced a special "Research Breakthrough" issue of its Chronicle. The Special Issue reported on the press conference on CFIDS held on 5th September 1990 in San Francisco, at which Dr Paul Cheney said: *"The most specific neurological symptom...is dysequilibrium. These patients have a balance disturbance and on certain simple neurological tests they fall over. On more sophisticated tests of vestibular function they're often grossly abnormal....Other evidence of central nervous system involvement can be demonstrated by tests looking directly at the central nervous system. These are slices of brain created by using magnetic resonance imaging. These inflammatory and/or demyelinating plaques can be seen in white matter, in the cerebellum and white matter tracks throughout the high cerebral convexities and in the frontal lobes. Over half of CFIDS patients will typically show lesions within the central nervous system....Switching from neurology to immunology, I want to show you what I believe to be the most striking immunologic defect in these patients. It is most convincing. This is the 2-5 A Synthetase/RNase L pathway....This system turns on and protects cells from viral infection and replication....This system is only turned on by a virus....In terms of severity, this is phenotypically unique to CFIDS....It's an absolutely striking observation suggesting a viral problem in these patients....These cells are infected with virus"*.

Dr Cheney then discussed biopsies from ME/CFS patients that showed an infiltration of mononuclear cells around small blood vessels within the deep dermis (causing, for example, loss of fingerprints). Cheney said *"It's called perivascularitis, or perivascular cuffing....What's interesting about this kind of lesion is that if this lesion occurred within the brain, in small vessels within the brain, it would produce many of the lesions we see on MRI scans. So I think that this pathology is not limited to fingertips. It can be found anywhere"*.

Wishing to make sure that the press corps understood how serious a disease ME/CFS is, Cheney continued: ***"I think it's really important for members of the press to recognise that what we're talking about here is not common fatigue....What we're talking about here in this systemic illness is that the debilitating fatigue is one of the primary symptoms, as it is in almost all autoimmune diseases and many other systemic diseases....We need to constantly separate out people who have common fatigue from people who have this illness"***.

At the conclusion of the press conference, when Drs Paul Cheney and David Bell were asked to comment on how seriously ill ME/CFS patients are, Dr Cheney said: ***"These patients' ...ability to experience life is destroyed. You see their entire social structures, work interactions and family units, come crashing down....It's an unbelievable illness"*** and Dr Bell said: ***"At the tip of the iceberg there are some patients who have it in extremely severe form and it can destroy their lives....So even without the injury caused by medical mismanagement, there's a very significant disability caused by this illness"***.

(Note: 23rd November 1990: Notes of the ME Study Group Meeting record that, in complete disregard of all this circulating biomedical evidence, contributors to a Press Briefing on ME by the Royal Society (one of the oldest scientific institutions in the world) that was designed to inform medical correspondents about ME emphasised the psychiatric approach: muscle abnormalities were stated to be secondary to inactivity, and reassurance, together with graduated exercise, were considered to be the best therapeutic approach. Psychological factors that pre-disposed, precipitated and perpetuated "fatigue" syndromes received considerable prominence, and one contributor attributed ME in children to school phobia).

1991: The Spring 1991 issue of The CFIDS Chronicle was a Conference Issue reporting on the CFIDS Association of America Research Conference held on 17th-18th November 1990 at Charlotte, North Carolina. Amongst the notable presentations were the following:

- Marc Iverson, President of the CFIDS Association, said in his Introductory Remarks: ***"The impact of this disease can be swift and relentless....I have never known a person with full-blown CFIDS who has not considered suicide at some point or points in his or her illness....The physical impact is often absolutely devastating. Pain, weakness, exhaustion, dizziness and more than another dozen other symptoms commonly occur....This intellectual impairment is truly bizarre... we have trouble finding words or our way home....Profoundly debilitated, intellectually compromised, unable to emerge from the haze, patients drop from sight....the things that matter to them – relationships, jobs, incomes, homes, families – slip through their fingers"***.
- Dr Paul Cheney (speaking about The Clinical and Epidemiological Features of CFIDS) said: ***"Early in the course...these patients exhibit disturbances in balance. You can perform simple neurologic tests in the clinic – Romberg and Tandem Stance. Patients will exhibit difficulties, even athletic individuals, and they'll be quite surprised at how they can't seem to stand up... if, in fact, they do not fall over"***.
- Dr Irina Rozovsky (speaking about Levels of Lymphocytes, Soluble Receptors & IL-2 Inhibitors in Sera from CFIDS Patients) said: ***"Chronic fatigue syndrome can be described as an immune dysregulative state, characterised by global immune upregulation with discrete immune defects....Normally T-helper cell activation is mediated by two intracellular signals. The first signal is the activation of protein kinase C....The second major signal for T-cell activation is the mobilisation of both cytotoxic and extracellular calcium. This activation finally leads to the secretion of interleukin-2 (IL-2) and the expression of IL-2 receptor on the surface of T cells....Soluble IL-2 receptors have been found in...sera from patients with multiple sclerosis, autoimmune diseases, AIDS, different types of lymphomas and leukaemias and in cancer patients who use IL-2 therapy. It is well-known that patients in IL-2 treatment have the same kind of symptomatology as our chronic fatigue syndrome patients....We have measured the levels of these soluble IL-2 receptors and T8 receptors in chronic fatigue syndrome patients....We have found that our patients have an elevated level of IL-2 receptor compared to healthy controls. Their level of soluble T8 receptor will also be significantly higher than for the control group....These two soluble***

receptors [IL-2 and T8 receptors], which reflect certain T-cell responses, could be very good markers for the disease and may even reflect the degree of severity of the illness”.

- Dr John Martin (speaking about Detection of Viral Sequences Using Gene Amplification) said: “(We have used PCR) in helping to establish that at least **a significant number of patients diagnosed as having CFIDS do have a persistent viral infection associated with neurological dysfunction, accompanying metabolic changes, and immunological changes**”.
- Dr Anthony Komaroff said: “**Our model for CFIDS is...that fundamentally, the illness involves a compromised immunity....This compromised immunity leads to a reactivation of latent viruses including HHV-6 and EBV. In some patients, it may well include the entero, coxsackie, echo, and even polio viruses....In other patients, environmental toxins could possibly compromise immunity....What all of the data indicates to me is something that will come as no surprise to any of you, and that is that CFIDS is not simply a state of mind**”.
- Dr Daniel Peterson said: “All of us who treat patients, I think, would agree that **there is a subset of patients with CFIDS who are really very disabled**. Their lives resemble nothing of their former lives; oftentimes they're bedridden. They interact with nobody....**I have been impressed...by how few patients are malingering, attempting to imitate this disease, or attempting to seek any secondary gains**”.
- Dr Robert Suhadolnik said: “The 2-5A synthetase/RNase L cell system is a mechanism by which we are able to defend ourselves from viral infections....**We have patients whose RNase L is completely shut down....As we were studying HIV-infected individuals, we found that the HIV retrovirus shuts down the RNase L. Had we not done those studies, we would not have had an explanation for what we're seeing here**”.
- Dr Jack Lieberman (speaking about serum ACE in ME/CFS, which is angiotensin-converting-enzyme, angiotensin being one of the main substances in the body that controls blood pressure) said: “An elevated serum ACE could very well be a marker for (ME)CFS....(Because high levels of ACE are found in sarcoidosis) a relationship of chronic fatigue syndrome to sarcoidosis must also be considered....**Elevation of serum ACE in patients with CFS lends credence to the concept that CFS is a true disease**”.
- Dr Denis Wakefield (an immunopathologist from Australia) said: “I do not think that we should blindly accept the CDC criteria for the diagnosis of this disease....Last year we published, in the Australian Medical Journal, a comprehensive study summarising the immunological abnormalities found in 100 CFS patients compared with age-and sex-matched controls. This group of patients had significant lymphopenia, which occurred in both the helper and suppressor T-cell subsets. They also had increased HLA DR antigen expression on the peripheral blood mononuclear cells....The primary reason your HLA DR antigen rises is because of interferon....**The major conclusion from this study is that the abnormalities that we have observed in the T-cell mediated immunity in people with CFS are not attributable to depression...most of our studies now indicate that the site of pathology in this disease must be within the central nervous system**”.
- Professor Nancy Klimas said: “**The most compelling finding was that natural killer cell cytotoxicity in chronic fatigue syndrome was as low as we have ever seen in any disease. This is very, very significant data with very, very low levels of lymphocyte response to mitogens....The actual function was very, very low – 9% cytotoxicity; the mean for the controls was 25. In early HIV and even well into ARC**

(AIDS-related complex) ***NK cytotoxicity might be around 13 or 14 percent....Chronic fatigue syndrome patients represent the lowest cytotoxicity of all populations we've studied***".

- In the moderated Question and Answer session, Dr Klimas warned that in almost every case, any psychiatrically active drug that has been tested has been shown to be immunosuppressive; she specifically warned against the side effects of Prozac (*"Prozac is anything but a benign drug. I would caution anyone who prescribes it to know a lot about the side effects of this drug"*); she warned against the use of the tricyclics in ME/CFS because they suppress immune function and **she pointedly warned against use of lithium -- a drug that Simon Wessely recommends for ME/CFS**.

(Note: Wessely is on record recommending lithium for people with ME: *"There is no doubt that at least half of CFS patients have a disorder of mood. The management of affective disorders is an essential part of the treatment of CFS/ME. Numerous trials attest to the efficacy of tricyclic antidepressants in the treatment of fatigue states. Patients who fail to respond should be treated along similar lines to those proposed for treatment-resistant depression. Adding a second antidepressant agent, especially lithium, may be beneficial"* (The chronic fatigue syndrome – myalgic encephalomyelitis or postviral fatigue. S Wessely PK Thomas. In: Recent Advances in Clinical Neurology (ed): Christopher Kennard. Churchill Livingstone 1990: pp 85-131).

It is of note that Professor Klimas wrote to Wessely warning him that his treatment would make ME patients worse: she informed him that her own immunological studies showed that anti-depressants must not be used for such patients due to their damaging effect on the immune system. She warned Wessely that lithium was particularly dangerous for people with ME, but Wessely ignored Professor Klimas' warning and went ahead with the use of antidepressants, including lithium, for patients with ME. This raises the issue of malpractice by Wessely, but the General Medical Council's stance, sent on 6th October 1993, is: *"The members have asked me to stress that the Council cannot take action against groups of doctors on the grounds that they hold particular views on medical issues"*. It is also a matter of record that a very severely affected young person with ME was admitted to King's College Hospital for a trial of their "wonderful new treatment". When she became worse, Wessely was informed. His reaction was *"Get her sectioned and we will give her ECT"* (electro-convulsive therapy). Her father picked her up and ran out of the hospital).

- Dr Byron Hyde said: ***"Brain mapping has started to change the ideas and the views of physicians across North America. Look at the primary manifestations of this disease – they reflect central nervous system damage....There are also major, major cardiac aspects of this disease"***.
- Dr Carol Jessop said: ***"I have been involved with CFIDS since 1983....I knew that what (my patients) were telling me was something very serious; it is one of the worst illnesses that I ever heard described to me before....Nausea...seems to increase as the illness goes on....balance problems increase in the chronic stages....98% of patients acutely complained of frequent urination.... Cold extremities are also very common....89% of the patients had irritable bowel syndrome....I am not the only one who has noted the high incidence of endometriosis....87% have fibromyositis. General abdominal tenderness was very common, in 80% of patients....Low magnesium levels are common....Low zinc levels are also common....Both of these trace minerals are absorbed in the gut and, I think, are being malabsorbed by our patients"***.
- Dr Alan Landay said: ***"We have found changes in three markers which seem to be the most significant. First, the CD 11 B marker, which identifies the suppressor cell, decreases in CFIDS patients....There is also an increase in the CD38 and the HLA DR indicating activation....Flow (cytometry) has been a useful tool for studying a number of diseases, including cancer, AIDS, and autoimmune disease. It can identify individuals with immune disorders by using a large panel of markers....Flow cytometry has revealed evidence of CD8 activation in CFIDS"***.

- Dr Jay Levy said: *“If you look at the activation markers, they are raised in both CFIDS and acute viral illness....Some individuals...will not be able to turn off that activated state. The agent remains as a constant thorn, forcing the immune system to be activated until the agent is eliminated. In these individuals, the immune system never returns to a normal resting state. So these people are in a state of chronic immune activation. What is the result of this chronic immune activation? If an activated white cell is doing its duty, it has to be producing a certain number of lymphokines or cytokines that are working to control the agent that is infecting the body. But these cytokines can have side effects....Cytokines affect the brain, the bowel, the muscle, the liver (which) one sees in CFIDS. So, increased cytokine activation can affect many different tissues in the body (and) can also cause reactivation of other viruses....There is much clinical information showing that (CFIDS) has often led to other immune diseases....The sequelae...include autoimmune disease and, on some occasions, MS”.*

Other speakers discussed functional brain imaging, sleep disorders, abnormal memory processes and speed, and **distinctive brain patterns seen in ME/CFS**.

1991: In March 1991 The CFIDS Association produced its first issue of **“Physicians’ Forum”**, with contributions from Drs David Bell, Paul Cheney, Jay Goldstein and Charles Lapp. The issue addressed the treatment of CFIDS/ME/CFS and the difficulties this posed because of the complexity and diversity of symptoms; topics covered included intramuscular gamma globulin, anti-inflammatory agents, calcium channel blockers, amplitgen, lifestyle adjustments, stress reduction and symptomatic treatment of specific symptoms. The over-riding message came from Dr David Bell: ***“The treatment strategies for CFIDS are still in their infancy, and very little progress will be made until the underlying cause or causes of the illness are clearly defined”.***

(**Note:** This view is not shared by UK psychiatrists of the Wessely School: Professor Wessely believes that research into aetiology is unnecessary: nine years later he stated: *“Some illnesses are treated without knowledge of the cause....examples include... chronic fatigue syndrome (CFS)”* – New research ideas in Chronic Fatigue. RSM Press; 2000. Another view expressed by the US physicians that is not shared by the Wessely School was the emphasis on the need to divide patients into several groups [mild to moderately affected, moderate symptoms but prolonged course, and those with severe symptoms], since the diversity in the clinical picture is the determining factor in symptomatic treatment, yet the Wessely School advocate a “one size fits all” regime of cognitive restructuring [to persuade patients with ME/CFS that they do not have a physical disease] combined with graded aerobic exercise and adjunctive antidepressants).

1991: On 16th April 1991, Dr Elaine DeFreitas addressed the US House of Representatives Committee on Energy and Subcommittee on Health and the Environment: ***“Let us note at the beginning that CFIDS or CFS/ME is not about being tired. Researchers have demonstrated numerous abnormalities of the immune, muscular, cardiovascular, and central nervous systems in people with CFS/ME; it is truly a multi-system disease with a strong component of immune dysfunction”.***

1991: Highlights of the Los Angeles Conference (Chronic Fatigue Syndrome: Current Theory and Treatment; Patient Advocacy Convention) held on 18th-19th May 1991 included presentation of new and important data (reported in The CFIDS Chronicle Fall 1991). Dr Ismael Mena, Director of the Division of Nuclear Medicine at Harbor-UCLA Medical Centre, presented data from SPECT scans of ME/CFS patients. He found ***“significant reduction in blood flow (hypoperfusion) of the temporal lobes amongst CFIDS patients. 70% had hypoperfusion of the temporal lobes, while 45% showed reduced blood flow in the frontal lobe. The parietal lobes of 40% of CFIDS patients indicated reduced blood flow. These results were obtained from SPECT scans taken while the patients were at rest....Dr Mena conducted a second study to determine if there were any differences in blood flow after exercise....Dr Mena summarised the result of this study by saying: ‘We saw a depression in cerebral blood flow after exercise when we should have observed an increase’. Temporal and frontal lobes seemed to be most affected by exercise. Hypoperfusion after exercise was more pronounced than that exhibited while patients were at rest”.***

Dr James Daly, Co-Director of the Exercise Physiology Laboratory and Director of the Harbor-UCLA Sleep Disorders Laboratory found that most CFIDS patients ***“had low normal maximal exercise capacity and oxygen consumption***

when compared to sedentary controls (the controls were “the most deconditioned people we could find”). In addition: ***“Several patients with no history of systemic hypertension demonstrated an exaggerated increase in blood pressure during exercise”***. Daly also found that ***“Many individuals, with no history of lung disease, had low CO₂ levels at rest. Low carbon dioxide levels lead to shortness of breath after any amount of exertion and might explain why some people with CFIDS experience bouts of ‘air hunger’ ”***.

1991: In August 1991 the ANZMES (Australia and New Zealand ME Society) magazine “Meeting Place” No: 36 published “Clinical Protocols from America” in which Dr David Bell said: ***“There is a huge spectrum of disease severity in CFIDS...Patients who have been ill for five years or longer, have prominent neurologic symptoms, and had a gradual onset of symptoms are less likely to experience spontaneous resolution of their symptoms....Unfortunately, there are patients who are very ill with CFIDS, many with very serious neurologic symptoms, where it is unlikely that they will spontaneously recover to a normal or near normal level of function....Very little progress will be made until the underlying cause or causes of the illness are clearly defined”***.

In the ANZMES article, Dr Anthony Komaroff from Harvard said: ***“Chronic fatigue syndrome represents a state of excessive cytokine production and therefore vitamin utilisation pathways may be partially blocked...SPECT scanning often reveals larger areas of low blood flow within the temporal lobes”***; Komaroff went on to mention the ***“pressure-like headaches and balance disturbances common to this disorder”***.

1992: The February 1992 issue of The CFIDS Chronicle carried on its front page a Statement from Dr Walter Gunn, Principal Investigator of CFS studies at the CDC (Centres for Disease Control): ***“Our Surveillance Study does not support the notion that CFS is a psychiatric illness, and in fact, suggests that it has an organic basis. Recent published reports suggest that the immune system may be involved in this illness. Additional published research suggests that viruses may also be involved in CFS”***.

1992: The September 1992 issue of The CFIDS Association’s Physicians’ Forum (entitled “CFIDS: The Diagnosis of a Distinct Illness”) carried important articles by key players in the ME/CFS stakes, including Drs David Bell, Paul Cheney, Charles Lapp and Nancy Klimas.

Dr Bell stressed the importance of a thorough physical examination and suggested an appropriate laboratory workup for those with suspected ME/CFS; he said: ***“Fatigue, sore throat, abdominal pain, headache, lymph node pain, myalgia and arthralgia suggest the presence of viral infection. Neurologic symptoms such as dizziness, balance disorder, paresthesias, and cognitive disturbances involving short-term memory and attention may be present....Neurological abnormalities may include hyper-reflexia in the lower extremities, Romberg’s sign and impaired tandem gait....Numerous immunologic abnormalities have been described in patients with chronic fatigue syndrome....Decreased natural killer cell function is perhaps the most reproducible immunologic abnormality”***. The seriousness of the disorder is reflected by the fact that Dr Bell listed the differential diagnoses as including rheumatoid arthritis, lupus erythematosus, Lyme disease, multiple sclerosis, sarcoidosis, hepatitis B, polymyalgia rheumatica, HIV virus infection and malignant disease, whilst Leonard Calabrese categorised the differential diagnoses as endocrinological (hypothyroidism, Addison’s disease, diabetes); rheumatological (fibromyalgia, Sjogren’s syndrome, polymyalgia rheumatica, polymyositis); neurological (obstructive sleep syndrome, multiple sclerosis); infectious (Lyme disease, HIV); haematological (anaemia, lymphoma) and renal, hepatic or cardiac disease.

In his presentation entitled “The Diagnosis of Chronic Fatigue Syndrome: An Assertive Approach” that was co-authored by Dr Charles Lapp, Dr Paul Cheney stressed the need for the case for diagnosis by objective criteria. He said: ***“The central problem is case selection. Many patients with CFS are excluded from studies because they seem ‘too sick’ to have CFS....CFS cases are mixed in with non-cases. Inappropriate controls are sometimes used. Some investigators, aware or unaware of a bias, attract or include in their studies the patients who best fit their view of CFS. This so-called selection bias can markedly affect the observations of a study....The medical evidence cited for CFS asserts that the following are present more or less in every patient during the course of his or her disease: T-cell activation, discrete immune defects, viral activation or re-activation, exercise-related dysfunction, and evidence of brain dysfunction or injury. While none of these tests can stand alone to ‘diagnose’ the illness, an array of these tests can be used to support this diagnosis”*** (it is worth recalling that in the UK, in

its 2007 Guidelines on “CFS/ME” which were strongly influenced by the Wessely School, NICE proscribed these tests).

Dr Paul Cheney then listed **22 physical findings in ME/CFS**, stating that *“Contrary to suggestions by some investigators, abnormalities on physical examination, although sometimes subtle, are usually present”*; he listed **10 routine laboratory tests that are often present in ME/CFS patients**; he listed **4 tests of immunity and 5 tests of discrete immune defects**; **5 tests of viral activation or re-activation**; **5 tests of exercise-related dysfunction**, and **tests of brain dysfunction (structural scans, functional scans and neuropsychometric tests, including the Halstead Reitan battery)**. Cheney continued: *“CFS clinical and bench researchers are developing an array of tests which are increasingly sensitive and specific for CFS – particularly when used in combination. **When patients present with symptoms that suggest CFS, we believe it is in their best interests to ...employ these tests to confirm the diagnosis and to document the nature and extent of each case. This information...enables the patient to make appropriate lifestyle adjustments (including defence of disability claims when necessary)**”*.

Cheney’s article was followed by a comprehensive overview as an aid to the diagnosis of ME/CFS by **Dr Jay Goldstein**, who addressed **skin disorders in ME/CFS**; **headaches**; **eye problems**; **ear, nose and throat problems**; **pulmonary complications** (*“Dyspnoea, either at rest or on exertion, is the most frequent [pulmonary] complaint, but is probably centrally mediated”*); **cardiac abnormalities** (*“coronary artery spasm and microvascular angina should be considered”*); **gastrointestinal problems** (*“Gastrointestinal complaints are very common, and symptoms of irritable bowel form an integral part of the CFS spectrum of symptoms”* – this should be compared with Professor Peter White’s assertion in 2006 that *“bowel symptoms are not part of CFS/ME”* (St Bartholomew’s Hospital Chronic Fatigue Services, Stakeholder comments on Chapter 6 of the draft NICE Guideline on “CFS/ME”, page 316); **pelvic disorders** (*“Perhaps the most common pelvic disorder in CFS is endometriosis....Adnexal masses and polycystic ovarian syndrome occur with greater frequency in CFS....A much higher percentage of my patients in a CFS practice have developed ovarian carcinoma that I experienced while practising family medicine”*); **genitourinary complaints** (*“Dysmenorrhea is also more common in CFS patients, even if endometriosis is not present....The primary genitourinary complaint in the male with CFS involves prostatic discomfort, frequency, and nocturia”*); **musculoskeletal abnormalities**; **neurologic abnormalities** (*“fasciculations are fairly common, as are tremors....A Hallpike test is sometimes abnormal in vertiginous patients, as is the Romberg test. Muscle weakness is common....Patients should be followed for the development of multiple sclerosis or, more commonly in my experience, immune polyneuropathy”*); **associated carpal tunnel syndrome (CFS) and thoracic outlet syndrome (TOS)** (*“carpal tunnel syndrome and thoracic outlet syndrome are fairly common in CFS”*); **haematological abnormalities** (*“CFS patients often complain of easy bruisability or spontaneous ecchymoses....Platelet function studies are sometime abnormal”*). Goldstein noted that: *“The SED rate is often very low. Immune complexes and positive anti-nuclear antibodies are encountered very frequently....Elevated levels of various cytokines and their receptors are often seen”*; he discussed at length the cytokine abnormalities found in ME/CFS and other distinct laboratory abnormalities, as well as SPECT scan abnormalities, evoked responses testing, PET scan abnormalities, lesions detectable by MRI scans, abnormalities on neuropsychological testing, and functional capacity evaluation (ie. an assessment of the patient’s ability to perform work demands and activities of daily living). Goldstein concluded by stating that he knew of no other mechanism than a limbic encephalopathy that could produce the diagnostic constellation seen in ME/CFS, but he pointed out that *“Secondary adrenal insufficiency due to a central mechanism relating to CRH deficiency could be responsible for many CFS symptoms”* (in which he specifically included vertigo, intermittent blurred vision and alopecia).

Professor Nancy Klimas wrote about **“Diagnosing CFIDS: An Immunologist’s Approach”**, saying: *“Our group in Miami has been actively working to better understand CFIDS since 1985....Some of this work has helped to develop a sense of diagnostic certainty in the evaluation of CFIDS patients, as well as to identify subgroups that are immunologically different from the majority of CFIDS patients....We have found the immune evaluation to be quite important, as it not only helps classify the patient, but often helps to direct the care of the patient”*. **Dr Klimas** went on to discuss the level of T-cell activation seen in ME/CFS patients, the diminished cell function, and the evidence of viral reactivation.

Other contributors to this issue of “Physicians’ Forum” who provided their expertise on the diagnostic approaches to ME/CFS included **James Jones** (*“Unfortunately, the group of individuals being given this diagnosis remains quite heterogeneous. Unless a common definition is applied to all patients...the heterogeneity of the population will preclude determination of diagnostic tests”*); **Anthony Komaroff** (*“Our studies also indicate that two additional tests are elevated more often in patients with CFIDS: **immune complexes and immunoglobulin G (IgG)**”*); **Benjamin Natelson** (*“The major lab tests I check are those indexing immunological dysfunction. I do a*

standard clinical immunological profile, including circulating immune complexes, complement levels and IgG subclasses...being able to report such examples of immune dysfunction is often of practical value in assisting the severely ill CFS patient in obtaining disability") and Daniel Peterson ("Often an objective measurement of the fatigue, such as one obtained through exercise tolerance testing with expired gas exchange, will document impaired VO2 utilisation. This documentation often helps to affirm the significance and extent of this aspect of the disease").

In the UK, all this evidence of serious organic disease fell – and continues to fall -- on the deliberately deaf ears of the Wessely School, the Medical Research Council and the NHS. Indeed, it was stated at the time that the Wessely School and UK clinicians would never accept the views of "people like Cheney" (personal communication).

1992: A Press Release for the Albany, New York, International Clinical and Research Conference on ME/CFS (held on 2nd-4th October 1992) from the **Department of Neurology, Institute of Neurological Science, University of Glasgow** said: *"We will report...our new findings relating particularly to enteroviral infection. We have now extended our PCR data to cover hundreds of patients together with controls and have continued to find a very significant proportion of the patients' muscle biopsies to contain enterovirus on PCR. In addition we have used several different types of enteroviral primers and have obtained identical results in the patients with these primers, the control muscle biopsies from healthy subjects and patients with other muscle diseases being entirely negative. We furthermore have isolated RNA from patients and probed this with large enterovirus probes which demonstrated that full length 7.4 kilobase virus was present in these patients. Indeed, detailed studies including Northern Blot analysis showed that the material was true virus....Furthermore, this virus was shown to be replicating normally at the level of transcription. Sequence analysis of this isolated material showed that it had 80% homology with coxsackie B viruses and 76% homology with poliomyelitis virus, demonstrating beyond doubt that the material was enterovirus. We were able to extend these studies...by being able to study post-mortem material from a definite case of chronic fatigue syndrome....This showed that enterovirus was present in skeletal muscle, in heart muscle, but particularly was abundant in brain. Detailed studies of the brain enterovirus revealed that it was most prevalent in diencephalic, particularly hypothalamic, regions. Clinical studies employing dynamic techniques of measuring neuroendocrine neurotransmitter hypothalamic function showed that there was disturbed hypothalamic regulation for neurotransmitters, particularly for 5-hydroxytryptamine and for hormones governing water metabolism in affected patients".*

1992: Scientists and clinicians at The Albany Conference discussed the epidemiology of ME/CFS, clinical research, viral studies, immunological studies, evidence of mitochondrial dysfunction, abnormal neuroendocrine responses, including defects in central control of respiration (ie. a defect in HPA axis function), evidence from ergometry with gas analysis which proves that patients are truly "weak", evidence establishing two gene markers that occur frequently in CFIDS patients but not in the general population (persons with HLA Dr4 and Dq1, who collectively represent less than 5% of the general population, were found in 93% of the ME/CFS population tested, and both markers are associated with decreased NK cell activity), ocular manifestations, and public policy, including the economic impact of ME/CFS. A review of the conference was published in The CFIDS Chronicle, Summer 1993. The full proceedings were published in the Journal of Clinical Infectious Diseases 1994;18: S1).

1993: In his now world-famous Testimony before the US FDA Scientific Advisory Committee on 18th February 1993, Dr Paul Cheney said: *"I have evaluated over 2,500 cases....We have seen the worst and the best of the range of scenarios that can befall a patient with this disorder. At best, it is a prolonged postviral syndrome with slow recovery or improvement within one to five years. At worst it is a nightmare of increasing disability with both physical and neurocognitive components. The worst cases have both an MS-like and an AIDS-like clinical appearance....We have lost five patients in the last six months....The most difficult thing to treat is the severe pain....The most alarming is the neurological and neurocognitive elements of this disease. Half have abnormal MRI scans, 80% have abnormal SPECT scans, 95% have abnormal cognitive evoked EEG brain maps. Most have abnormal neurologic examinations....40% have impaired cutaneous skin test responses to multiple antigens. Most have evidence of T-cell activation....From an economic standpoint, this disease is a disaster. 80% of the cases evaluated in my clinic are unable to work or attend school...The yearly case production, if*

plotted, is exponential....The medico-legal aspects of our practice steadily grow as this disease eats at the fabric of our communities. We admit regularly to the hospital (with)...inability to care for self....CFS is an emerging, poorly understood disorder with a distinctive clinical presentation... This disorder is a socio-economic as well as medical catastrophe that will not end....This disease is too complex to rely on standard medical orthodoxy to explain it....Listen to patients with an open mind. Failing that, then listen to those who have spent countless hours with a thousand patients. Most of us have some wisdom to impart and most of that came from patients”.

1993: The Los Angeles conference entitled “The Medical Neurobiology of Chronic Fatigue Syndrome and Fibromyalgia” was held on 7th-9th May 1993 and reported in the Summer 1993 CFIDS Chronicle. Emphasis was again placed upon the importance of brain scans, with **the most talked-about technology being the results of Dr Ismael Mena’s SPECT scans (conventional brain scans such as MRI and CT scans look at brain structure over function, but SPECT scanning examines brain function by measuring cerebral blood flow or CBF).** Results showed profound dysfunction in CFIDS patients: **“We are seeing a pattern of blood flow that is quite different from the uniform pattern of distribution that we see in the normal individual....CFIDS is characterised by a diminution of CBF and diminished uptake of HMPAO (a radioisotope used to track CBF), primarily in the right hemisphere, extensively involving the frontal and the temporal lobes....The study of CBF and its relationship to cerebral function appears to be a very powerful biological marker for CFS”** (brain imaging for NHS patients with ME/CFS is not available in the UK and requests are refused). The CFIDS article continued: **“Cerebral hypoperfusion is the most common finding in the CFIDS brain, and researchers have associated it with nearly every CFIDS symptom”.** Drs Mena and Goldstein presented a series of SPECT scans **“which showed extreme hypoperfusion in the brain following exercise. There appeared to be ‘holes’ where blood would normally be flowing – the degree of hypoperfusion was astonishing. Even 24 hours later, cerebral blood flow was severely reduced”.** Dr Byron Hyde from Canada said: **“What we’re going to tell the insurance companies from now on is not ME, for which they won’t pay, and not CFS, but major acquired brain dysfunction. And that is what these people actually have”.**

Other researchers drew attention to the presence of vertigo in patients with ME/CFS, which is **“probably the result of the reactivation of viruses caused by the dysregulated immune system”**, according to Dr Samuel Whitaker from UC Irvine; to a central defect in the HPA axis that **“prevents the immune system from shutting down, and results in constant immune activation which makes people with CFIDS feel sick”** according to Dr Anthony Komaroff from Harvard. Drs Lapp and Goldstein noted a particular irregularity in tidal volume in CFIDS patients **“This phenomenon has never been described before in any population and...we think that it’s a diagnostic marker for CFS”**. The Cheney-Lapp study showed that neuroendocrine responses were often reversed or blunted; Drs Lapp and Sietsema reported that people with CFIDS reached anaerobic threshold much sooner than predicted.

A major section of the conference addressed the immune defects in CFIDS patients: **“Up-regulation of the immune system has been well-documented in the CFIDS literature....That this immune activation is responsible for many CFIDS symptoms has been accepted by most researchers and physicians”.** Dr Catherine Rivier from the Salk Institute in La Jolla, California, said: **“Stress in any form places undue pressure on the immune system....In a normal immune system, interleukin (IL-1) is produced in response to stress. In CFIDS, IL-1 may be obstructed, resulting in a blockage of corticotropin releasing factor (CRF), an immunosuppressor. If CRF is not released, the immune system will remain activated indefinitely”.** Dr Nancy Klimas said: **“In a normal population, 20 percent of lymphocytes are active at any given time. In CFS, up to 80 percent of the cells are working....These lymphocytes and cytokines are so up-regulated that they cannot be driven any harder. It is as if they have been pushed as far as they can go and the immune system is completely exhausted”.**

1993: The Summer 1993 issue of The CFIDS Chronicle Research Update carried a referenced article by Dr Paul Cheney in which he noted the evidence of metabolic disorder in ME/CFS: **“CFS patients demonstrate low oxygen consumption, early transition to anaerobic metabolism, disordered fat metabolism and sweet cravings which fit well into a picture of mitochondrial dysfunction....Evidence of liver dysfunction has recently been observed in most CFS cases. Liver dysfunction would explain the medication and chemical sensitivities so common to CFS. Gut dysfunction, especially increased gut permeability, is presumed to be the basis of cellular energy deficiency and is common to CFS. This would compound the effects of liver dysfunction and could also explain such diverse complaints as food sensitivities or allergies, irritable bowel syndrome, chronic nausea and**

arthralgias....Reduction in cellular ATP would profoundly affect cellular active transport systems....Electrolyte and mineral gradients would decline and result in further loss of critical cell functions. Intracellular magnesium deficiency reported in CFS would be one of the many examples of this phenomenon....Most interesting of all, liver dysfunction as well as central nervous system mitochondrial dysfunction could explain the subacute encephalopathy so common to CFS. Indeed, cognitive-evoked computer brain maps of severely ill CFS patients are entirely consistent with a metabolic encephalopathy including that seen in hepatic encephalopathy....CFS patients crave carbohydrates (but) if they eat fat, they cannot consume it in the mitochondria, due at least in part to acylcarnitine deficiency, and therefore fat storage increases, as does body weight. Serum cholesterol and triglycerides rise in some individuals...The loss of excess intracellular minerals such as magnesium due to reduced cellular ATP and subsequent reduced active transport is a special problem....Cardiac function, as well as muscle function in general, may also be profoundly affected by intracellular magnesium deficiency”.

1993: In The CFIDS Chronicle Physician’s Forum, Fall 1993, Dr James McCoy from Louisiana wrote: **“A dysfunctional immune system may be related to the failure of other organ systems frequently observed in CFIDS....Some CFIDS patients produce very low levels of DHEA (dehydroepiandrosterone, a naturally-produced hormone and a precursor of oestrogen and testosterone in humans)....Many CFIDS patients are very sensitive to medications and do not tolerate normally-recommended dose levels. Many drug agents, including DHEA, are toxic to CFIDS patients’ lymphocytes at routinely-prescribed dose levels”.**

The same Chronicle devoted considerable space to the issue of multiple chemical sensitivity (MCS) in people with CFIDS (ME/CFS): **“...some chemicals are more likely to cause MCS than others. These include dry cleaning fluids, car exhaust, pollution, solvents, paints, new carpet, perfume, smoke, fire, drugs, organic and inorganic chemicals. Commonly seen pollutants which may cause brain dysfunction include acetone, trichloroethylene and chlorinated hydrocarbons”.**

Two important points were made in that issue of Physicians’ Forum; Dr Robert Sinaiko from San Francisco mentioned something that is very common but frequently dismissed by uninformed physicians: “Many CFIDS patients experience lower right abdominal pain, which I hypothesise is mycotic mesenteric adenitis, an inflammation of the lymph nodes in the abdomen as a result of immune activation”, whilst Vicky Carpmann pointed out: “Autoimmunity is commonly seen in CFIDS....Once an autoimmune condition begins, it cannot be reversed”.

1994: In its issue of Winter 1994 (ie. early 1994), the CFIDS Chronicle reported on meetings in September 1993 at the CDC and on a two-day workshop held in November 1993 at the NIH on the clinical management of ME/CFS. **Dr Dedra Buchwald listed commonly reported symptoms not included in the case definition, notably shortness of breath, unsteadiness, morning stiffness, blurred vision and dizziness, and she noted the presence of multiple chemical sensitivity.** She stated that **“improvement may represent an accommodation of limitations rather than a disappearance of symptoms”.** **Dr Anthony Komaroff provided a review of the respiratory, neurological, rheumatic and gastro-intestinal symptoms of ME/CFS, and emphasised that he did not find that ME/CFS patients over-report symptoms that are not common to the illness. Dr Jonathan Rest reminded clinicians that patients are usually more sick than they appear.**

1994: The International Meeting on Chronic Fatigue Syndrome was held in Dublin on 18th-20th May 1994 under the auspices of the World Federation of Neurology. There were 24 poster presentations and 46 verbal presentations, including those by **Dr Anthony Komaroff** from Harvard Medical School, Boston, (who spoke on case definitions); **Dr Paul Levine** from the National Cancer Institute, Maryland (the history and epidemiology); **Dr Irving Salit** from the University of Toronto (precipitating events); **Professor Ted Dinan** from London (the neuroendocrinology of the disease); **Dr Charles Poser** from Harvard (the differential diagnosis between ME/CFS and MS); **Dr Frances Aitchison** from Glasgow (brain scans on ME/CFS patients); **Dr Jay Goldstein** from California (cerebral blood flow [CBF] by SPECT scans); **Dr Russell Lane** from Charing Cross Hospital Medical School, London (defective muscle metabolism and the presence of enterovirus RNA in the muscle); **Dr Wilhelmina Behan** from Glasgow (mitochondrial changes); **Dr Hirohiko Kuratsune** from Osaka University, Japan (acylcarnitine deficiency); **Dr T Majeed** from the Department of Neurology, University of Glasgow (who also spoke on abnormal intracellular acylcarnitine); **Dr Layinka Swinburn** from the Department of Chemical Pathology and Immunology, St James University Hospital, Leeds (insufficient ATP and the consequences); **Professor Andrew Smith** from the University

of Bristol (abnormalities in objective measures of cognitive impairment), and **Professor Dr Rainer Ihle** from Dusseldorf (immunological changes, hormonal disturbance and increased levels of toxins, and on myocardial SPECT scans).

Dr Anthony Komaroff said that symptoms which are not currently part of the case definition such as anorexia, nausea, alcohol intolerance and parasthesias may be added to a revised case definition.

Dr Jay Goldstein from Los Angeles had done hundreds of brain scans on ME/CFS patients and reported that SPECT scans show obvious abnormalities. He said that the overall patterns of rCBF (regional cerebral blood flow) were distinctly different in depression compared with CFS, and that **patients with (ME)CFS who have co-morbid fibromyalgia have more severe hypoperfusion than patients with (ME)CFS alone. He said it is possible to differentiate (ME)CFS from depression by looking at the hypoperfusion pattern**

Dr Frances Aitchison, a radiologist from Scotland, said that she had performed both MRI and SPECT scans on ME/CFS patients and that **the abnormalities related to areas of hypoperfusion (ie. low oxygenation levels); the areas are principally in the temporal lobes, occipital lobe and the left frontal lobe and these abnormalities are statistically significant.**

Dr Russell Lane, a neurologist from London, reported on exercise studies done by his group and said that **32% of (ME)CFS patients tested had abnormal SATET responses (sub-anaerobic threshold exercise testing) suggesting defective muscle metabolism and 21% were positive for enterovirus in muscle**; there was a significant association between abnormal SATET and enterovirus (being greatest in patients with a greater lactic acid response to exercise). **Heart rate response to exercise, as well as muscle fibre morphometry, showed these abnormal lactate responses could not be due to deconditioning; he stressed that morphologically, most of the (ME)CFS patients had muscle hypertrophy, whereas unused or deconditioned muscles would be expected to show atrophy. He concluded that a significant proportion of ME/CFS patients have evidence of impaired aerobic muscle function.**

Dr John Gow from Glasgow reported that **evidence of enteroviral sequences can be found in the muscles of up to 82% of (ME)CFS patients and that the persistence of a virus may upset cell homeostasis.**

Dr Wilhelmina Behan from Glasgow said that **electron microscopy has shown abnormalities of mitochondria: enlargement, change of shape and proliferation of cristae, giving an abnormal honeycomb appearance, was found in up to 70% of muscle biopsies (the abnormal mitochondria were about twice the size of normal).** The structure of mitochondria is very closely linked to energy metabolism and Dr Behan concluded that the findings suggest an interference with energy metabolism. **Cell cultures were established from 10 muscle biopsies and severe decrease in cell respiration was found in two of the four samples tested. Serum acylcarnitine is deficient in CFS patients. A mtDNA deletion was found in four patients but in none of the controls.**

Professor Dr Rainer Ihle from Germany said that **data on 375 CFS patients demonstrated various immunological changes and autoantibodies (especially antinuclear antibody and microsomal thyroid antibodies) in an abnormally large proportion of CFS patients, suggesting impaired immunity and facilitating transition to autoimmune disease ("On the basis of these immunological serological and organ-specific findings, which affirm previously published results, it would appear that the organic nature of the pathogenesis of CFS has now been demonstrated").** SPECT scans showed reduced rCBF in 83%, and MRI scans showed focal changes in 30%. SPECT scans of the myocardium showed conspicuous changes in 73% during exercise. Professor Ihle reported that 75% of his cohort experienced dizziness and 53% had hair loss. He said that future studies should differentiate subgroups of CFS, which would improve targeting of therapies.

Dr Layinka Swinburne from Leeds confirmed that **the distinct symptom of ME is fatigability of muscle after minimal exercise, with slow recovery before muscle power is restored.** She presented evidence that the basis of the fatigability is a defect in the regeneration of high energy phosphates, especially ATP, and that such an impairment would generate changes in membrane bound transport and ion movement, leading to chronic intracellular ion depletion (phosphate, potassium and magnesium), with further impairment of mitochondrial function; **physical activity would produce greater depletion, leading to interference with many other functions such as immune reactions, hepatic detoxification, gut motility, neurotransmitter function, maintenance of red cell shape and tissue respiration.**

Dr Sean Coyle, an associate of Dr Swinburne, noted that **serum potassium and phosphate levels have been shown to be decreased in ME and that renal tubular handling of phosphate was low, suggesting an inappropriate loss of phosphate in patients with ME. He noted that low phosphate levels could affect every cell**

in the body and may cause bone fractures, weakness, fatigue, abnormal pulmonary function, low blood pressure and depressed cardiac stroke volume, as well as cognitive dysfunction.

Dr Jay Levy from San Francisco presented **serological and immunological data from (ME)CFS patients, pointing out that, by lymphocyte phenotype analysis, the T8 suppressor subset was decreased, a notable and important finding.** He also found that activated T cells were increased, with the most pronounced increases seen in the sickest patients, and that **NK cell activity and cytotoxic lymphocyte activity were both depressed in (ME)CFS patients.**

Dr Hirohiko Kuratsune from Japan expanded on his 1992 presentation at the Albany, New York; he found that most ME/CFS patients – male and female -- had serum acylcarnitine (AC) deficiency, and that **the degree of AC deficiency related to the severity of the symptoms; no AC deficiency was found in bed-rest patients without ME.CFS, implying that low AC in ME/CFS patients is not due to physical deconditioning.** He pointed out that the sicker patients have lower AC levels. There was no urinary increase in AC, thus the deficiency could not be attributed to urinary loss.

Dr Charles Poser from the US, an internationally renowned neurologist specialising in MS, **found similar brain lesions in both ME/CFS and MS patients, suggesting a chronic and recurring brain disorder. In his view, the fatigue in both disorders is indistinguishable. He reported authoritatively that atypical reactions to many different medicines and drugs is virtually pathognomonic of ME/CFS.**

Professor Ted Dinan from London reported on **abnormal neuroendocrine findings** and said that **the pattern of neuroendocrinological response appears to be unique in ME/CFS patients**, with an enhanced prolactin (an important stress hormone) response when challenged by the anti-anxiety drug buspirone, and a blunted response to dexamethasone, with ME/CFS patients having lower baseline GH (growth hormone) levels than either normal controls or depressed patients.

Professor Andrew Smith from Bristol said that over 5 or 6 years **he had demonstrated significant impairments of motor function and abnormalities on objective measures of memory and attention, and that central nervous system functioning is definitely abnormal in ME/CFS patients.**

Professor Mark Demitrack, a US psychiatrist, reported that patients with major affective disorders tend to have hypercortisolism, whereas patients with (ME)CFS have adrenal insufficiency (ie. hypocortisolism), with a 30% drop in overall cortisol output. He concluded that **“(ME)CFS patients cannot be absorbed into any pre-existing psychiatric diagnostic category”.**

(Note: The Dublin meeting was an important international conference, but apart from derisory comments in the medical trade press, it received almost no mention in the medical journals or mainstream media. The medical trade press was factually incorrect and scathing: “GP Magazine” carried an article by Paul Haines with banner headlines proclaiming: *“Research fails to impress”*, which went on to disparage the entire conference: *“In Dublin last month, when the city hosted the first world conference on myalgic encephalomyelitis (this was incorrect – the first was held four years previously in April 1990 at the University of Cambridge), one old woman claimed to know the condition’s origin...Her point of view was only slightly less conventional than many of the other theories that were expounded at the conference...The American presence was enormous, reflecting the enthusiasm with which that country has embraced the subject of ME. Three or four delegates carried video cameras to record each other....Each speaker presented his pet theory with some research data to back it up. But once the talk was over....there seemed little lasting interest....There were countless presentations about viral triggers and neuro-endocrine activity”*. Despite the biomedical evidence that was presented, the article erroneously asserted: *“Disappointed doctors are none the wiser after ME conference”*. Commenting on an Editorial in “GP”, Dr Shepherd of the ME Association said *“the editorial went on to describe, quite inaccurately, a meeting attended by ‘hundreds of hangers-on’ and papers being presented by ‘those who measured and pampered the afflicted’”*. Later that same year, on 20th November the Sunday Telegraph reported on **a conference attended by 150 British psychiatrists held on the island of Jersey, proclaiming: “ME is just a myth....A group of leading psychiatrists has overwhelmingly concluded that ME is all in the mind”**).

1994: The Spring 1994 issue of the CFIDS Chronicle carried an article by Dr Paul Cheney of Charlotte, North Carolina, on the likely pathophysiological mechanisms underpinning ME/CFS, in which **he drew attention to key symptoms. These most commonly include...subnormal temperature; myalgias (especially of axial skeletal muscles); deep bone pain in the extremities; arthralgias; pressure headaches; sleep disorders; enlarged and/or**

painful lymph nodes; night sweats; new onset or worsening of allergies; dizziness or balance problems; migrating sensory dysesthesias; sensitivities to heat, cold, light, sound and chemicals; alcohol, food and drug intolerance; visual disturbances; disabling cognitive impairments; acneform, herpetiform and morbilliform skin eruptions, and an assortment of breathing, cardiac, gastro-intestinal and genitourinary symptoms.

Amongst the most common physical findings (ie. signs detectable by a clinician) are palpable, slightly enlarged discoid-shaped and tender posterior and middle cervical lymph nodes, which are almost always left-side predominant. This left-sided predominance and lymphatic channel tenderness extending into the medial supraclavicular area strongly suggests increased lymph production – lymphatic fluid carries cytokines, and in an immune activation state, lymphatic flow increases, causing fluid retention and tissue oedema commonly seen in ME/CFS which would produce lymphatic congestion (over 90% of lymph flows back into the blood stream just below the left collar-bone, so if there is increased flow, congestion will occur within lymph node chains closest to that juncture, hence left-sided dominance of lymph node tenderness in the supraclavicular area).

Other common physical findings include a higher than normal incidence of hyper-reflexia (80% of patients) and abnormalities of vestibular function with an inability to maintain the Romberg, tandem or augmented tandem stance positions (which clinically support the evidence of central nervous system injury observed on functional and structural brain scans).

In an interview with Dr Cheney published in the same issue, he said that **ME/CFS patients have limited anti-oxidant reserve, and this is why exercise sends them into relapse.**

The same issue carried an article by Dr Nancy Klimas et al reporting on the association between HLA (histocompatibility locus antigen) Class II antigens and CFIDS/ME/CFS. Klimas noted that her group and others have reported a strong association between immune dysfunction and a serological viral reactivation pattern in these patients similar to that observed in conditions such as chronic active hepatitis and systemic lupus erythematosus in which a definite association between a particular HLA-DR/DQ haplotype and increased disease frequency has been reported. Her data suggest that DR4 and DR5 are associated with an increased risk of developing CFIDS/ME/CFS and that it may be triggered in such people by various stimuli, resulting in a state of chronic immune dysequilibrium. This would easily explain the findings with regard to acute viral infections, chronic active viral infections and allergies in these patients.

1994: The Summer issue of CFIDS Chronicle carried an important article by Professor Paul Cheney explaining exactly why the 2'-5' A / RNase L pathway is so important in (ME) CFS: noting the clinical impression that patients suffer from a chronic viral infection, Cheney stated: ***"Perhaps the strongest evidence that (ME)CFS may be due to a persistent viral infection is the strong activation in (ME)CFS patients of a principal anti-viral pathway. The 2'-5' A synthetase/RNase L pathway is the most important intracellular antiviral defence mechanism in mammalian cells....It is initiated by alpha interferon expressed by activated T cells.***

"The alpha interferon binds to receptors on the surface membranes of most cells in the body. This receptor binding results in the expression and activation of 2'-5' A synthetase, which converts ATP (a source of energy) to bio-active 2'-5'-oligoadenylates (2'-5' A). Ultimately, this pathway activates RNase L...to degrade human and viral single-stranded RNA.

"Significant activation of RNase L would substantially disrupt cell metabolism and energy production and beyond that, organ and body function.

"Hormonal action in the body would also be substantially disrupted by activation of RNase L. A clinical situation could arise in which patients appear to be hypothyroid or hypocortisolaemic, based on clinical signs and symptoms, even though their actual hormone levels were normal.

"Disruption of messenger RNA by RNase L would, in effect, functionally decapitate hormone function at the cellular level.

"This problem would not necessarily respond to hormone therapy, even if the patient clearly had clinical evidence of hypocortisolaemia or hypothyroidism.

"Additional cell functions could be affected including the production of neurotransmitters within the brain, detoxification enzymes within the liver and digestive enzymes within the GI tract.

“In other words, there would be a ‘brown-out’ of organ function and body systems. The action of RNase L could explain the myriad organ system problems seen in (ME)CFS and could well be the cause of the severe and debilitating fatigue in this disorder.

“Alpha interferon, in addition to activating the 2’-5’ A / RNase L pathway, could cause specific injury to ...the brain. Alpha interferon is known to be a potent neurotoxin acting through the μ -opioid receptor in the brain to provoke specific neurotoxic injury to deep brain structures.

“Alpha interferon injected into rat brains is known to specifically injure the HPA axis with a resulting decline in corticotropin-releasing hormone (CRH) production. A decline in the HPA axis has been demonstrated in (ME)CFS patients.

Alpha interferon can cause extensive deep brain injury and may be the common denominator in explaining why (ME)CFS and AIDS dementia complexes show almost identical injury to deep brain structures.

“In summary, the alpha interferon/2’-5’A/RNase L pathway, if upregulated, would cause two problems which are ubiquitous to patients with (ME)CFS: substantial cellular metabolic dysfunction with profound fatigue; and severe neurocognitive problems due to deep brain injury.

“At this time, activation of the alpha interferon / 2’-5’ A / RNase L pathway is the best common denominator to explain why people with (ME)CFS are sick”.

1994: The Fall issue of the CFIDS Chronicle published questions and answers in the section “Ask the Doctor”. One such was the reply provided by Professor Anthony Komaroff from Harvard, who is also Chief of the General Medicine Division at Brigham & Women’s Hospital, Boston, as well as leading a research team for one of the three NIH-funded CFS Co-operative Research Centres. **In reply to the question “Why do (ME)CFS patients tend to relapse after exercise?”, Komaroff was clear: “this is due to an unusual reaction of the immune system to exercise”.** He went on to explain that: ***“Research groups around the world continue to report that the (ME)CFS patient’s immune system seems to be in a chronically stimulated state, as if it is engaged in a battle against something it perceives as foreign to the body. Even though the immune system is often in a chronically-stimulated state, some parts of the system seem not to be working very well --- perhaps because they have been working too hard”.*** In reply to the question ***“Is there any evidence that (ME)CFS is caused by an infectious agent?”***, Komaroff stated: ***“In my judgment, the leading candidates continue to be enteroviruses, herpesviruses...and retroviruses”.***

In an article titled “Immune Dysfunction in CFIDS: Why You Feel the Way You Do”, **Dr Robert Keller** from the Centre for Special Immunology, Miami, explained: ***“Most chronic states of immune dysfunction have, as a necessary requisite, a genetic component. This genetic ‘failing’ occurs in a region known as immune response genes, or the HLA system....recent evidence suggests that CFIDS shares this genetic quirk with other chronic immune activation disorders such as systemic lupus erythematosus (and) chronic active hepatitis.***

“Whatever the nature of the trigger....in CFIDS, as in all states of chronic immune activation, the initial presentation of the insulting agent to the cells of the immune system precludes its initial destruction or its effective control. As a result...the immune system remains unbalanced as it tries, albeit unsuccessfully, to rid the body of the insulting agent. A major consequence of this unbalanced condition is the persistent production of powerful cytokines. At some point, this continuous production exceeds the ability of the body to inactivate them. This, in turn, results in their systemic dissemination and a variety of unpleasant consequences....The ability of these cytokines to interact with receptors that are involved in central nervous system control creates many other untoward results. It is now recognised that the brain, the endocrine system and the immune system represent an inextricably linked triad. Imbalance in any one of these ‘linked’ systems, therefore, will result in obligatory disturbances of the other two”.

1994: A four-day International Research and Clinical Conference co-sponsored by the American Association for Chronic Fatigue Syndrome (AACFS) was held in Ft Lauderdale, Florida, on 7th – 10th October 1994; it was also sponsored by the NIH, the CDC and the University of Miami. It was reported in the UK ME Associations’ magazine “Perspectives” in March 1995 and in the CFIDS Chronicle in January 1995 (from which some of these comments are taken with grateful acknowledgement). **Of the 475 conference participants, nearly half were clinicians and researchers.**

The Conference was in two parts, these being the research section held on 7th – 9th October 1994 and the clinical section held on 9th and 10th October 1994.

Knowledge about ME/CFS that was available in 1994 includes the following:

Dr James Jones of Denver, Colorado, reported on exercise capacity testing and **the finding of reduced exercise capacity, including abnormal muscle strength and higher than expected heart rate, as well as high lactate levels in (ME)CFS patients.**

Dr J Vercoulen from Nijmegen found that **patients with (ME)CFS had significantly lower levels of physical activity than healthy controls and that these were similar to patients with MS.**

Dr Alison Mawle from the CDC reported that **patients with (ME)CFS suffer from higher rates of allergy-related symptoms than normal controls and these were present in 70% of patients investigated.**

Dr Adrienne Bennett from Brigham & Women's Hospital, Boston, measured transforming growth factor beta (TGF β) and found that it was elevated in (ME)CFS patients, which might reflect the body's attempt to down-regulate an over-active immune system.

Dr Roberto Patarca (an immunologist from the University of Miami) pointed out that there was growing consensus that many of the viruses observed in (ME)CFS may not be relevant to the aetiology but nonetheless relevant to the pathology that is seen.

Dr Richard Lanham of the State University of New York at Buffalo reported **a very high frequency (stated as 100%) of eye complaints amongst (ME)CFS patients studied.** Post-onset symptoms included photosensitivity; photophobia; sensation of foreign body in the eye; blurry vision; abnormalities of peripheral vision; trouble reading; ocular pain; headache; floaters; double vision; itchiness and hazy vision (some of which could be due to fatigue of the eye muscles). Problems seen on ophthalmic examination included narrowed arterioles; retinal defect; fibrillar changes in the vitreous; peripheral cystoid degeneration; drusen; pigment changes; chorioretinal macular abnormalities; pavestone degeneration and optic pallor (this being indicative of neurological disease). Examination of the patients found that 38% had abnormalities of the fundus; 50% had inflamed eyelids and 41% had other pathologies. **Dr Lanham also reported that a significantly greater number of patients than controls had a family member with an autoimmune disease (65% versus 21% of controls). He further reported that (ME)CFS patients have stiff RBC (red blood cell) membranes like those seen in end-stage renal disease patients, and that this may represent a unique marker for (ME)CFS: "(ME)CFS patients' stiff RBCs 'may not traverse nutrient capillaries well, resulting in cellular hypoxia...this defect may be part of a more extensive membrane abnormality' which may affect neurons and other cells, leading to additional symptoms"** (it is notable that there is now clear evidence of disrupted biology at cell membrane level and of **abnormal vascular biology, with disrupted endothelial function in both large and small arteries, pointing to increased cardiovascular risk for people with ME/CFS** – Int J Cardiol 2011;doi:10.1016/j.ijcard.2011.10.030).

Dr Daniel Clauw from Georgetown University Medical Centre, Washington, discussed the relationship between interstitial cystitis (IC) and (ME)CFS: *"IC may be yet another disorder which has considerable clinical and pathogenic overlap with FM and (ME)CFS"*. In relation to the overlap between the two disorders fibromyalgia and ME/CFS, Dr Clauw **noted the gastrointestinal symptoms and chest pain frequently described by patients (hence the need to use accurate diagnostic criteria, as called for by Dr Patarca).**

Dr Lawrence Borish from the National Jewish Centre for Immunology, Denver, measured TNF- α , IL-1, IL-6 and IL-10 (all associated with lethargy and inflammation); they found that TNF- α and INF- α (interferon alpha) were increased in ME/CFS patients but decreased in major depression. Most remarkably, IL-10 was absent in ME/CFS patients (IL-10 is produced by all T-helper cells and is stimulated by TNF- α , the presence of which implies an inflammatory reaction). **The absence of IL-10 supports the characterisation of ME/CFS as an immune disorder with a defect in the immune system's ability to suppress the on-going immune reaction.**

Dr Adrienne Bennett from Boston measured TGF- β (a suppressor cytokine) in serum from patients with ME/CFS, from those with depression, with lupus and with healthy controls; levels were significantly elevated in people with ME/CFS compared with the other groups. High levels of TGF- β may be the immune system's attempt to suppress immune up-regulation (whilst some parts of the immune system are down-regulated, others are up-regulated: **Dr Joseph Cannon** from Pennsylvania State University provided historical and scientific evidence that **females are more resistant to infection than males because of an up-regulation of the immune**

system; however, it is because of this up-regulation that women are more susceptible to autoimmune diseases).

Dr Irving Salit from Toronto General Hospital found that **the percentage of CD4 (T-helper cells) was increased in ME/CFS patients** compared with chronically fatigued controls who did not meet the CDC case definition for ME/CFS (a finding that is seen in people with allergies). **He determined that ME/CFS patients have “a variety of immunologic abnormalities (including deviations in) immunoglobulins, T lymphocyte subsets and cell mediated immunity”.**

Drs Roberto Patarca, Nancy Klimas and Mary Ann Fletcher et al described three groups of ME/CFS patients based on patterns of cytokine dysregulation: (1) dysregulation of TNF- α/β expression in association with changes in serum levels of IL-1 α , IL-4, (soluble) IL-2R and IL-1 receptor agonist; peripheral blood mononuclear cell-associated expression of IL-1 β , IL-6 and TNF- β messenger RNA, and T-cell activation; (2) inter-related and dysregulated expression of soluble TNF receptor types 1, (s)IL-6R and β 2-microglobulin, and significantly decreased lympho-proliferative activity; (3) significantly decreased NK cell cytotoxic activity.

Dr Kenny De Meirleir from Brussels studied 149 patients with ME/CFS, categorising patients' functional abilities using the Karnofsky Performance Scale (KS) which scores from 100 (perfectly well) to 0 (dead). 56 ME/CFS patients had a functional ability of less than 65 and 62 scored between 65 and 75. Flow cytometry was used to measure cellular immune status and **the majority of immune abnormalities were found in the ME/CFS group with KS scores between 65 and 75. The immune abnormalities included increases in CD3+HLA-DR+ve T cells and an increase in the CD4/CD8 ratio (an increase in this ratio is found in allergies); there was also a decrease in NK cells.**

Dr Daniel Hamilos from the National Jewish Centre for Immunology, Denver, **demonstrated abnormalities of the autonomic nervous system in (ME)CFS patients compared with depressed patients and normal controls and he suggested that this was further evidence for distinct patho-physiologies in (ME)CFS and depression.**

Dr Daniel Clauw from Washington, DC, looked at inflammatory symptoms of the upper respiratory tract and bladder, postulating that central nervous system hyper-activity leads to ‘**neurogenic inflammation**’, this being an inflammatory response mediated by the release of neuropeptides such as Substance P and that this increased level of Substance P *“came from nerves within the bladder and may be responsible for the irritative symptomatology seen in (ME)CFS and FM”.*

Drs Anthony Komaroff and Adrienne Bennet et al concluded that *“despite their clinical similarities, FM and (ME)CFS are characterised by different abnormalities of the somatotropic neuroendocrine axis”.*

William Pettibon, MA; LMHC from the Centre for Special immunology, Ft Lauderdale, found that the results of his neuropsychological study reinforced the view that (ME)CFS patients were not malingering; together with Dr Nancy Klimas et al **he found specific areas of cognitive dysfunction, including verbal memory; verbal attention/concentration; visual attention/concentration; visual memory; mental flexibility; rate of memory acquisition and in the level of overall cognitive functioning.**

Dr Benjamin Fischler from Brussels compared SPECT scans of patients with (ME)CFS versus those with depression and normal controls; **cerebral blood flow was significantly reduced in (ME)CFS patients compared with the other two groups.**

Dr Frances Aitchison from Glasgow presented additional neuroimaging evidence of differences in blood flow in specific areas of the brain from that which she had presented in Dublin earlier in the year, this being **the presence of abnormalities not seen in controls, and evidence that these abnormalities correlated with specific symptom severity.**

Dr Frank Duffy from Harvard Medical School, Boston, described quantitative electroencephalogram (qEEG) findings in patients with (ME)CFS compared with depressed patients and normal controls. **Spike waves were seen in 44% of (ME)CFS patients versus 1.3% of the other groups, most commonly in the temporal region. (ME)CFS patients had significantly more sharp waves and frequent bursts of high amplitude alpha and theta waves in the posterior regions. Dr Duffy suggested that these abnormalities provide indirect evidence of an inflammatory process of the central nervous system, spike and sharp waves being indications of CNS irritability.**

Dr Charles Lapp from Charlotte, North Carolina, suggested that EEG neurofeedback (phase reversals, increased slow wave activity, decreased fast wave activity and an increased amplitude of the brain wave upon cognitive challenge) could serve as a diagnostic marker for (ME)CFS.

Dr E. Pizzigallo from Chieti, Italy, carried out muscle biopsies from the vastus lateralis muscle in (ME)CFS patients and found alterations in the tissue *“compatible with a myopathy of probable mitochondrial origin”*, which might account for the decreased functional capacity of muscles in (ME)CFS patients.

Dr James Jones from Denver reported that **maximum oxygen consumption, maximum workload and anaerobic threshold were reduced in (ME)CFS patients, suggesting that cardiac function at maximal exercise may be abnormal in (ME)CFS.** He also performed isometric muscle studies in the quadriceps and hamstring muscles which showed that knee flexor fatigue, strength and recovery were decreased when compared to body weight in (ME)CFS patients. He commented that these dysfunctions may be caused by *“intrinsic cardiac disease or abnormality in the vascular supply or metabolism of the muscles in the lower extremities”*.

Dr J Vercoulen from the Netherlands compared an assessment of physical activity in 51 (ME)CFS patients, 50 fatigued MS patients and 53 healthy subjects; **(ME)CFS and MS patients scored similarly and significantly lower than controls on the actometer worn at the ankle 24 hours daily for two weeks.**

Notable short quotes from the question-and-answer session of the clinical conference include the following:

Dr Paul Cheney (in response to questions about gastrointestinal symptoms in ME/CFS): *“Many of these patients are immune activated and may have leaky guts. Undigested food protein leaks across the gut and patients develop reactions to it....CFIDS patients seem to have problems with detoxification, which may explain their sensitivity to medications. We are trying to improve liver function to increase tolerance of medications.....A recent study at The Cheney Clinic demonstrated that the sickest patients did not respond well to any therapy”*.

Dr Anthony Komaroff (responding to the question: *“What causes problems with focusing the eye in CFIDS?”*): *“There may be intermittent dysfunction of the ciliary muscles, which attach to the lens of the eye. If those muscles are not working well, the lens can’t adequately change shape and things become blurry”*.

Dr Paul Cheney (replying to the request *“Please discuss the neurological aspects of CFIDS”*): ***“There is evidence of functional neurological injury in patients with CFIDS as demonstrated by hyper-reflexia, clonus, balance disturbance and brain irritability”***.

Dr James Jones: *“I think the SED rate (the ESR rate in the UK) can be a fooler. There are a number of individuals who have inflammatory type symptoms, but their SED rate is absolutely normal. The SED rate is an old, non-specific test of inflammation which is dependent on fibrinogen and interleukin-6. But if inflammatory processes are activated in other ways, the SED rate can be perfectly normal...a normal or low SED rate does not exclude an inflammatory illness”*.

Dr Nancy Klimas (when asked about the advisability of people with ME/CFS having flu/hepatitis B or live vaccines): *“Personally, I don’t use live vaccines in any of my patients with immune disorders”*. **Dr James Jones** added: *“There are very few live vaccines that adults need”*.

Dr James Jones (replying to a question about allergies in ME/CFS: *“Is allergy a common denominator?”*): *“Clinically, this appears to be so....There is literature that suggests that allergic patients, when they get sick, have more symptoms and are sicker longer than other individuals”*.

Dr Anthony Komaroff: *“ANA (antinuclear antibody) tests are abnormal more often”*.

Dr Nancy Klimas (replying to the question *“Is there any link between endometriosis and CFIDS?”*): *“I see a higher incidence of endometriosis in my CFIDS patients than in my general clinic patients”* and **Dr Anthony Komaroff** said: *“We have just done a case-control study...preliminary results indicate that there may be a higher frequency of endometriosis in the CFIDS patients versus the controls”*.

Dr Sharon Moss: ***“The type of cognitive deficits seen in CFIDS patients are similar to those of aphasia, traumatic brain injury and dementia patients”***.

From the Doctor-to-Doctor session: “The leaders of the session felt that it was extremely important to validate the patient’s illness”.

(Note: The Wessely School profoundly disagree with such a view: they are on record in 1992 asserting at the CIBA Foundation Symposium on ME/CFS that the first duty of the doctor is to avoid legitimisation of ME/CFS patients’ symptoms, a situation that, disturbingly, continues to date in the UK).

The current situation in the UK

The above illustrations provide historic evidence of the organicity of ME. Current research confirms the organicity, for example, Professor Chris Ponting from the University of Edinburgh has just published an article in the EMBO (European Molecular Biology Organisation) Journal *Molecular Medicine*: **“Replicated blood-based biomarkers for myalgic encephalomyelitis not explicable by inactivity”**. A press release from the University of Edinburgh states: **“The largest ever biological study of ME/CFS has identified consistent blood differences associated with chronic inflammation, insulin resistance and liver disease”**. The study found that individuals with post-exertional malaise (PEM – the hall-mark symptom of ME) show stronger biomarker differences. Professor Ponting said: **“For so long people with ME/CFS have been told that it’s all in their head. It’s not. We see it in their blood”**. He said the evidence should **“dispel any lingering perception that ME/CFS is caused by deconditioning and exercise intolerance”** (www.bbc.com/news/articles/cy8k73443g4o).

Despite all the evidence of the organicity of ME, as of June 2025 the situation in the UK for people with ME (and also for one in every two people with Long Covid who fulfil the strict diagnostic criteria for authentic ME) is more dire than ever.

For the avoidance of doubt, there is no shortage of published evidence that the Wessely School regards the terms “ME” and “CFS” as synonymous. Confirmation of this is the letter sent on 10th October 1993 by psychiatrist Dr Peter White to Dr Mansel Aylward at the DSS:

“I was worried to learn that the Disability Handbook ‘will probably conclude that myalgic encephalomyelitis is a separate entity within the group of disorders encompassed by the chronic fatigue syndromes and that affected people remain disabled, make little or no progress, or even deteriorate over time’. I am a psychiatrist who has been studying fatigue (and) I would not agree that there is a consensus that ‘ME’ and the chronic fatigue syndrome are separate conditions...I suggest that separating the two conditions may enhance disability. The reason for this is that those who believe in the separate existence of ‘ME’ believe this is a totally physical condition, probably related to immune dysfunction or persistent viral infection (for) which no treatment is available. On the contrary, I think present evidence suggests that the chronic fatigue syndrome is...a discrete syndrome and treatments and rehabilitation programmes are available which address both the physical (and) psychological factors that maintain this syndrome. For this reason, I would ask you to reconsider separating the two conditions”.

There can be no doubt about the intention of the Wessely School psychiatrists: *“In the Guide to Mental Health in Primary Care, Professor Wessely includes ME as a mental disorder, whilst on the King’s College website it asserts that ‘CFS has officially replaced the term ME’, when such is not the case under the auspices of the WHO (and) Collaborating Centres are not permitted to change classifications without the approval of the World Health Assembly”* (letter dated 18th August 2003 from the Countess of Mar to Dr George Szumukler, Dean of Psychiatry at the Institute of Psychiatry).

Mindful of the intentions of the Wessely School, it may be unsurprising that in the same month that Professor Ponting published his research findings confirming replicated blood-based biomarkers for ME, as mentioned on page 1, Elsevier published the 11th edition of Kumar & Clark’s standard medical text book “Clinical Medicine”, in which ME is placed in the Psychiatry section under MUS and FND (Medically Unexplained Symptoms and Functional Neurological Disorders).

The text is misleading, for example:

“...several studies have demonstrated abnormalities in endocrine, neurological, and immunological parameters in patients with CFS”: no mention is made of the cardiovascular, musculoskeletal or gastrointestinal abnormalities; there are many thousands, not “several”, published biomedical papers on ME/CFS

“Delivering and expanding a positive diagnosis of MUS/FND is the stepping stone towards a successful management plan that may include...CBT. Recovery depends on a positive patient engagement with the process”: it is internationally acknowledged that there is no “successful management” but, by implication, the patient is to

be held responsible for their lack of recovery if they are not positive about the recommended but out-dated psychosocial treatments

"Psychological treatments (such as CBT) are proven to reduce symptom burden...combined with acknowledging behavioural change to reduce avoidance": this is unequivocally erroneous and demonstrates that the author has disregarded the extensive published evidence that contradicts their assertion

"Personalised integrated care plans may incorporate psychological therapies (e.g., CBT, psychosocial interventions (e.g., pragmatic active rehabilitation programmes), and drug therapies (e.g., antidepressant medications)" : it is unclear how *"pragmatic active rehabilitation"* differs from graded exercise therapy (GET), which NICE has decreed should not be used because the studies upon which it relies are of *"low or very low"* quality and it has repeatedly been shown to be harmful to people with ME.

Doctors are specifically encouraged to read the PACE Trial, which has been exposed as fraudulent.

The take-home message is that CFS/ME sufferers should accept a psychological element to their illness.

In summary, the entry is incorrect to teach that ME is a functional neurological disorder when it is a formally classified neurological disorder. Such misrepresentation of reality is likely to cause iatrogenic harm to people with ME.

Given what has been known and shown about ME/CFS for so many years, how is it even conceivable that the Wessely School's comprehensively disproven psychosocial dogma is still embedded throughout the NHS, that the substantive biomedical evidence is ignored, that medical students and clinicians are still being misinformed, and that the revised NICE Guidelines have been rejected by the Medical Royal Colleges?