

Data or Dogma?

Margaret Williams 16th August 2014

A significant paper on the nature of ME/CFS was recently published: it concluded: ***“These data are consistent with evidence of multisystem dysregulation in CFS and implicate the involvement of DNA modifications in CFS pathology”*** (de Vega WC, Vernon SC, McGowan PO. DNA Methylation Modifications Associated with Chronic Fatigue Syndrome. PLoS ONE 9(8):e104757. doi:10.1371/journal.pone.0104757; published 11th August 2014, volume 9, Issue 8).

Of note is the authors’ description of ME/CFS as ***“a serious and debilitating disorder characterised by a constellation of physical symptoms and is known to occur following infection”***.

The diagnosis of ME/CFS was based on the Fukuda and the Canadian criteria, with the authors noting that: ***“CFS dysfunctions may involve multiple systems, including neuroendocrine, autonomic, metabolic and neurobiological”***.

The accompanying press release states that the researchers found evidence of distinct epigenetic profiles in immune and other physiologically relevant genes, explaining that epigenetic modifications affect the way genes are turned on or off without changing the inherited gene sequences: ***“These types of changes would be expected to affect immune cell function in ME/CFS patients....it is further demonstration of the indisputable biological basis of ME/CFS”*** (Solve ME/CFS Initiative: Breaking News: Chemical Changes in Immune Cell DNA from ME/CFS Patients).

Immediately apparent is the significant discrepancy between this evidence and the selectively published results of the PACE trial, as the cohort was essentially the same age group as PACE participants (in this study, ME/CFS patients’ age averaged 41.1 years and controls averaged 39.7 years, compared with the average age of 38 years in the PACE trial).

Comparison of the physical function scores of this study with the PACE trial is illuminating: in this study, the mean physical function score for patients was 38.9 but for the healthy age-and-sex matched controls it was 95.0. The standard error of the mean (similar to a standard deviation) was 1.5, giving a normal range of greater than 93.5.

In contrast, the PACE trial Investigators did not use healthy age-and-sex matched controls and decreed that a physical function score of 60 or higher represented the normal range (which meant that it was possible for a PACE participant to enter the trial with a physical function score of 65, then deteriorate physically over the course of the trial, yet still be reported as having “recovered” with CBT and GET).

There is something very seriously wrong here, yet Professor Peter White refuses all legitimate requests to release the raw data (which he does not own, as it belongs to UK tax-payers): this might be interpreted as his fear that if he did so, it would quickly be shown that the PACE trial was a resounding failure.

Although the multisystemic symptomatology of ME/CFS has been relentlessly dismissed by the Wessely School as evidence of psychosomatic disorder (***“The greater the number of symptoms and the greater the perceived disability, the more likely clinicians are to identify psychological, behavioural or social contributors to illness”***). Chronic fatigue syndrome: Symptom and Syndrome. Wessely S. Ann Intern Med 2001;134: 9S:838-843), it is well-documented and it fits with current evidence of multisystem dysregulation supported by the recent paper.

In the 1980s, there were three publications of note: (i) “Living with Myalgic Encephalomyelitis” by Mollie Mendelssohn, published by the UK ME Association in 1980; reprinted in 1981, 1982, 1983 and 1988; (ii) “The Mile-High Staircase” by Toni Jeffreys, published by Hodder & Stoughton in 1982, and (iii) “Myalgic Encephalomyelitis – Post-Viral Fatigue Syndrome and how to cope with it” by Dr Celia Wookey published by Croom Helm in 1986; reprinted in 1988 and 1989 by Chapman & Hall.

Given the now-proven evidence of multisystem dysregulation in ME/CFS, it may be salutary to quote a few extracts from these publications because they describe so convincingly the devastating reality of ME/CFS symptomatology that no caring clinician could justifiably ignore or dismiss, let alone advise that no investigations should be carried out, as was the case with the Joint Royal Colleges’ Report on CFS: ***“The group within CFS with more symptoms, profounder fatigability, greater disability and longer illness duration is the subset with the strongest associations with psychological disorder....The possibility that abnormalities of immune function play a role in the pathogenesis of CFS has attracted considerable attention. Such abnormalities should not deflect the clinicians from the biospsychosocial (ie. psychiatric) approach and should not focus attention towards a search for an ‘organic’ cause....No investigations should be performed to confirm the diagnosis”*** (Chronic Fatigue Syndrome. Report of a Joint Working Group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners. October 1996 Simon Wessely, Anthony David, Peter White et al).

(i) *"For over twenty years I had known that I was suffering from...a peculiar recurring virus...and I learned to live with what was then only a temporarily disabling condition. Suddenly...my life changed drastically. I was on holiday in the French Pyrenees...admiring the magnificent mountain scenery when I had a spasm in my coronary arteries....It became obvious within a few months that I was not making a normal recovery and was beginning to manifest new symptoms. I was in a perpetual state of uncontrollable exhaustion, when the slightest activity was too much. Holding a cup or fork was like being asked to hold a bag of cement. The joints of my lower limbs particularly were swollen, extremely painful, and alternated between being fiery hot or icy cold, with trembling. I wept copiously for no reason at all. I had extraordinary rashes, almost anywhere, preceded by a lot of pain, the sort of pain one might associate with shingles...My leg muscles seemed to tire almost as soon as I started to move about, and my arms and hands too were affected....My physical balance was impaired....I developed neuritis, with bizarre electric shock type pains grabbing me out of the blue....It was pretty frightening and excruciatingly painful....My legs felt like pillars of lead.....I was unable to concentrate on anything of an intellectual nature....Muscular spasms came at any time....the really extreme exhaustion came back and I reverted swiftly to a collapsed state....The total unpredictability of the disease was obvious. It was apparent to me and everyone else that with this disease one couldn't win, either with complete bed rest or forced activity"* (Mollie Mendelssohn, Deputy Head of a Comprehensive School).

(ii) *"Suddenly, an iron hand grabbed something delicate in my midriff, and twisted it into a knot of pain...I seemed to be slowing down. It was the stairs first....the stairs got steeper....It was more of a general weakness...I was done in....Gradually I discovered (that) it was an uphill world. Everywhere I went there were stairs, stairs, stairs....The world was a flight of stairs....All the other joints were hurting too. From the large hip joints to the little ones in the fingers, none escaped. There was an ache in every muscle.... I had to pull myself upstairs by my arms. My legs were heavy.... When there was no way I could get up a stair alone, and riding in a car was sheer hell, I stopped going to work....I was a shaking pulp....My head buzzed....There was a pain in the back of my neck and across the shoulders. My chest was tight with a nagging pain. My lungs had turned to lead....Eating, drinking and talking were difficult....The mouth ulcers either went with the illness or were a reaction to the drug I was taking for the joint pains.*

"I lay in bed one evening, pain searing every joint and muscle....My chest caved in. Lightning shot through it. Pain darted down my arm. There was tingling in every limb....By this time I'd reached a stage of weakness where I could hardly walk....I sank to the floor...feeling very ill....The breasts were so painful I couldn't bear them to be touched....I thought I was dying that night. The pains were excruciating. The illness overpowered me. My feet were ice. And there was a new and agonising symptom. A burning pain in the chest....In the mornings I would wake up shocked. Shocked to find myself so unutterably not myself.

"There was no-one we could turn to.....If we kept the blood-sugar level up, I didn't seem to be dying quite so much....What I wanted to say to everybody was, 'For God's sake help me. I feel as if I'm dying'....I was physically unable NOT to cry. This is a peculiar phenomenon that occurs with excessive weakness. (A patient) told me that her husband, who had terminal lung cancer, wept when he was 'extra weak'. She knew what I meant, but nobody else did....No-one could feel like this and NOT die....On the way back to the ward I begged the attendant...not to bump me on the walls of the lift. I felt as though one bump would finish me off....My weakness was indescribably profound....Gradually I had to accept an unpleasant reality. That I wasn't just ill, I was helpless....An agony of sickness, weakness and fear...seemed to strangle me....Noises, talking to people, being in a car, the commotion of a hospital. All were bad for me....In allopathic or conventional medicine, tests results are crucial. Without a positive test, there can be no diagnosis. Without a diagnosis, illness doesn't exist....Tests were coming back negative....the laboratory could not lie. But a patient could.....How was it possible that one could feel ill enough to be convinced that death was close, yet the laboratory says, 'This patient is 100 percent well'?....I realised something about my eyes was different. They were behaving strangely....(Reading) made me feel sicker. Television was worse....We understand now that the disease affects the central nervous system and can damage the optic nerve, as well as the eye muscle, but we didn't know it then. That was when I couldn't cope. On top of the illness... I wasn't seeing properly.

"Through those terrible months, we began to notice that the illness had a pattern....After a relapse, I would have two or three weeks of hell – extreme weakness, sickness, a harsh buzzing in the head, and sometimes severe pain in the back of the neck and shoulders....One thing we knew. Rest was imperative. Activity was fatal.

"I was tired of being ill...But most of all I was tired to death of being judged by a succession of ...over-confident, smug male doctors from whom I had been forced to beg for help. But once again, I made the effort to be rational, charming, and light-hearted....Mustn't appear depressed. Must be so marvellously well-balanced that even eight months of shocking ill-health hadn't made a dent in my mentally healthy optimism....The next day (Dr) Jolly bounced back into the ward. 'Now', he said, 'Dr Eisenhower has confirmed my view that your illness is psychosomatic; (he) will give you lithium. Then you'll start to get better'.....Lying there crying I reflected on my perpetual naivety. I should have known better than to hope for anything from a psychiatrist...They make their living from mental disturbance....I was a sitting duck for their nonsense.

"All my life I had enjoyed being alone, but now I was afraid to be alone....One Sunday I found I couldn't cope....But who could I turn to? Who on earth would understand?....The weakness and sickness was so profound....But I was not only ill...the nightmare was back...I couldn't accept it. I was aghast....Any attack on my immune system could plunge me into serious illness....Every effort I made made me sicker.

“Altogether, the state of illness adds up to nothing positive for sufferers. One would indeed have to be insane to go through it all for nothing....But what is happening today is that perfectly sane people are given a diagnosis that could in common sense apply only to the genuinely insane....Modern medicine...has been over-selling itself for years....It will be up to the epidemiologists of the next century to sift the mound of facts and figures, the evidence. But they will never have before them the sum total of all the bungling, the errors, the unnecessary suicides, for these things are often hidden”. (Toni Jeffreys, an Australian medical facility researcher, who graphically portrays the problem that pervades modern medicine, namely, that it is no longer considered necessary to pay heed to the patient’s presenting symptomatology, only to basic laboratory results; if those are normal, then the symptomatology is not legitimate. As she says: **“An illness DOES NOT EXIST until the medical profession says it does. That is their intolerable power”**. This makes the Wessely School mantra all the more alarming: in 1992 they gave directions that in ME/CFS, the first duty of the doctor is to avoid legitimisation of symptoms [MRC Summary of the CIBA Foundation Symposium on CFS, 12th -14th May 1992, ref: S1528/1]).

(iii) In his 1986 Foreword to Dr Wookey’s book, Dr Melvin Ramsay said: *“I am in no doubt that in the very near future it will be fully established that ME is an organically determined entity and I hope that this book will aid our understanding of the condition”*. In an Additional Note at Reprint in 1988, Dr Wookey said: *“An impressive paper has been produced by Dr EG Dowsett and Dr Eleanor Bell (J Hosp Infect: March 1988) which makes out a very persuasive case for...enteroviruses being responsible for the protean symptomatology which has baffled so many experts...Drs Dowsett and Bell suggest that the chronic and relapsing nature of the condition can be explained by the continuing presence of the virus in tissues like peripheral muscle, the heart, central nervous system, liver, pancreas, thyroid, joints and sometimes the ovaries and testes”*.

Part I of the book deals with the history and nature of the illness; its clinical presentation; an explanation of immunology relating to allergies in ME; diagnosis and differential diagnosis, and management and research possibilities. Part II contains eleven typical case histories and a bibliography of literature on ME.

“Clinical Presentation: The initial symptoms may be an attack of vomiting and diarrhoea or a sore throat...Some time later the patient quite suddenly feels weak and collapses, and frequently says that he has never felt so ill in his life. He has no energy, his muscles feels like jelly and there may be severe pain in the back, legs, arms, chest or stomach....Among other symptoms that can appear are dizziness, giddiness, pins and needles or numbness, coldness of the extremities, muscle twitching, shivering attacks, palpitations, clumsiness, difficulty in sleeping and alternating moods.

Other important symptoms from the diagnostic point of view are given as: headache; pain in the back of the neck; sore eyes; sensitivity to light; legs feeling heavy; difficulty in standing; difficulty in carrying heavy weights or lifting arms above head; loss of appetite; nausea; loss of memory/concentration; spontaneous bruising; stiffness of neck; pain in abdomen; abnormal bowel movements; abdominal distension; excessive flatulence; blurred vision; pain in chest; tremor; sensitivity to noise; frequent crying; nightmares; shortness of breath; rashes; painful joints; frequency of micturition; dry mouth; flushing, and “feeling awful”.

Attention is drawn in particular to the role of the pancreas in ME, which could be crucial: *“Many patients present with severe stomach pain thought to be psychosomatic because of the apparent absence of confirmatory physical signs. But this is typical of acute pancreatitis. Professor William Philpott of Oklahoma has suggested that the pancreas may be a primary target organ in cases of autoimmune disease. If a virus attacks the pancreas, there may be a deficiency of pancreatic juices so that proteins are inadequately digested. They may therefore pass through the lining of the small intestine as undigested particles, and as such be attacked by the white cells in the patient’s blood stream as foreign bodies. The resulting large particle is called an immune complex and may cause blockage of the small blood vessels in the brain and elsewhere. This would explain the protean symptomatology of ME (which has led so many doctors to dismiss sufferers as hypochondriacs)...since the symptom produced would be dependant on the site at which the blood vessel was blocked”.*

Dr Wookey quotes from a 1985 paper by Professor Peter Behan et al in which they examined 50 patients: *“The results reported here suggest that the syndrome is due to the interaction of viral infection and immunological processes which produce damage to intracellular enzymes and result in abnormal muscle metabolism, especially on exercise”.*

Extracts from the case histories leave no doubt about the devastating nature of ME:

Case History 1 (M.W.): *“Any food caused immediate abdominal discomfort and I got the pain at times even when I was not eating....One callous nurse actually said that it was an idea I had formed in my mind that I had this pain...I was hypersensitive to noise and other peoples’ visitors were hell....I could not concentrate on reading or writing or even listening to the radio....the staff refused to believe that...my legs were too weak to walk as far as the canteen...the charge nurse was...adamant that the stick was merely a psychological crutch”.*

Case History 3 (Dr M.W.): *“The onset was insidious and the presenting symptom was palpitations....I felt weak and had a vague pain in my left arm....I also remember one or two attacks of uncontrollable shivering....I had a recurrence of the abdominal pain, more severe than before (and) it was*

accompanied by diarrhoea of up to six to eight times an hour....I was feeling really dreadful and... did not care whether I lived or died....All I cared about was that this suffering should cease....Fleeting symptoms included a sharp pain in my thumb joint and pain in the left side of my chest....I became aware of shortness of breath....The muscle weakness was so severe at times that I had to ask a nurse to help me cross...to the washbasin....Symptoms of autonomic disturbance included temperature changes, profuse sweating at times, pallor and palpitations...(I also had) 'the shakes'....The anorexia, lassitude and muscle weakness persisted. The pain was aggravated by food, which often provoked diarrhoea...and the passage of flatus....A new and disquieting symptom appeared in the form of giddiness (which) was worse on bending and worse with my eyes shut....My handwriting was almost illegible....The pattern of symptoms forming a relapse was usually the same. Sometimes I had a warning in the shape of an unexplained attack of diarrhoea...This was followed by profound muscular weakness, particularly affecting the legs, so that I could not stand for any length of time. Anorexia and nausea were prominent features (and I had)...a shivering attack like a rigor....The giddiness was extreme....Blurring of vision (meant that) I could not focus sufficiently to write...Facial ache resembling toothache or trigeminal neuralgia came and went, as did a tremor of the right hand...I cannot carry heavy shopping....I also get an aching pain in the back of my neck if I am sitting for a long time....Unlike multiple sclerosis, ME has encephalitic features such as loss of memory (and) concentration that in some ways make it even harder to bear" (the late Dr Celia Wookey, a former GP who used the pseudonym Dr Margaret White).

Case History 4 (J.G.): *"I was working as a nursing sister in the casualty department...with only four days sick leave in 18 years...I developed 'flu-like' symptoms one weekend....On returning to work, I felt unwell most of the time, with headaches, dizziness and staggering. Three weeks later...I suddenly felt as though I was going to die. The feeling came over me suddenly and I did not feel as though I would get home....I developed hypertension....(Four months later) when I was sitting watching television, I suffered what felt to me like a coronary spasm. My head felt queer, I became cold and sweaty and again thought I was going to die....I was prescribed anti-inflammatory drugs which aggravated my circulatory problems and made me feel worse....I suffered further episodes of circulatory spasms, hypertension, tingling, myalgia, abnormal bruising, fatigue, unsteady gait, mood swings, extreme pallor, sleep disturbance, angina, cold extremities, visual disturbance....I quickly went downhill and felt absolutely dreadful....I felt completely demoralised – here I was with a nice home, loving husband and family, a job which I enjoyed, everything to live for in fact, finding it very difficult to live through the misery, pain and uncertainty of each day....I was having problems with the medication. The dose was adjusted, but still I felt worse taking it...The medication had to be stopped....If I took a simple headache tablet or vitamin supplement I became really ill....Back in Northwick Park Hospital with a different team of doctors who were unable to understand my problem, I was again labelled neurotic and sent home".*

Case History 10 (J.C. – a mother and former full-time secondary school teacher): *"I was aware of a strange pain in my groin....I felt indefinably unwell....Whilst I was making the bed...the room reeled and I could do nothing but collapse on the bed feeling sick and indescribably ill...I tried to explain (to my GP) that I felt unwell all the time but that suddenly I would feel drained and desperately ill, as*

though I was fighting to stay alive....By now my legs and back ached as well as my arms, neck, head, ears and eyes. I had suddenly become photophobic....Even to talk was an effort....I felt palpitations...there was a build-up of extreme pain at the base of my skull and top of my arms and rib cage, with the occasional twitching muscle in the leg or shoulder blade. My vision was as if in a dream, grey and difficult to focus....I became covered in red spots from head to toe....I walked up the steep incline to the house feeling more and more unwell, sat down, and was hit again by excruciating pains, especially in my chest and arms. I felt faint with a terrible malaise and sudden exhaustion...as though my life was draining away...I was advised that going back to work would be a good rehabilitation....After a netball lesson I walked along the corridor to the foot of the stairs leading to the staff room and I knew I couldn't climb them. My body slid down the wall to the floor....At last our GP returned with ...a neurologist (who) walked towards me and said, 'You mustn't allow imaginary illnesses to get you down – you look perfectly healthy to me', and with that he playfully slapped me on the arm. It hurt and I was already so angry that I blindly struck out sideways, hitting him hard on the chest and sending him reeling.... I heard the GP apologising for me all the way downstairs....I seemed to feel tearful all the time and permanently exhausted....Every movement was such a painful effort that I couldn't stop crying....Small noises were like an electric shock to my system....I felt as if my legs were heavy and yet jelly-like and my body was bruised all over as though hit by small hammers....No balance, seasickness, nausea, my eyes refusing to focus and my ears and eyes telling me that I couldn't bear the noise and movement for another moment....A friend with ME said something to me that has haunted me, 'Generally people only face death once in a lifetime, but with this illness I go through the sensation of dying so often'....For the last few years I rise...generally nauseated with slight tummy pains and diarrhoea....Why do I sometimes experience acute giddiness that nearly knocks me off my chair? What is the reason for the nausea; diarrhoea; earache; blurred vision; aching eyes, arms, legs, neck, head and back; numerous facets of tenderness; swollen throat sensations; forgetting a common word in mid-sentence; muscle tremors; burning or swollen joints; tearfulness; cold extremities; headaches; abdominal pains (and) extreme exhaustion? When standing for more than two minutes, I always have to lean on something....The constant aching exhaustion all over, sudden shooting pains anywhere with no warning....Any sudden noise triggered uncontrollable tremors. To be sociable was a real strain, the effort of talking and listening was immense".

These case histories tell the truth about ME. It is not simply "chronic fatigue" from which recovery is possible with cognitive restructuring and aerobic exercise to dispel alleged deconditioning and hypervigilance to normal bodily sensations. A school of thought that continually ignores evidence of multisystem dysregulation because it is contrary to the central precept of their own doctrine can make no claim to be practising medical science.

<http://www.meactionuk.org.uk>