Short synopsis of "CAUSES OF SYMPTOMS AND SYMPTOM PERSISTENCE IN LONG COVID AND MYALGIC ENCEPHALOMYELITIS/CHRONIC FATIGUE SYNDROME" by PROFESSORS ANTHONY KOMAROFF (Harvard) and ROBERT DANTZER (University of Texas) published in August 2025

Margaret Williams August 2026

NOTE: whilst this is intended as a short synopsis of the above Review, in order to understand the significance and importance of the Review, it is deemed essential to provide the background to the orthodoxy in the UK.

There is increasing evidence that ME/CFS and Long Covid overlap and that ME is an autoimmune disorder. The above publication in Cell Reports Medicine (19th August 2025 https://doi.org/10.1016/j.xcrm.2025.102259) further substantiates such evidence. The Review was funded by the US National Institutes of Health and by The University of Texas.

The quoted extracts provide clear examples of the biomedical evidence which unquestionably disproves and discredits the erroneous, scientifically-unsupported beliefs and teachings of certain influential psychiatrists known as The Wessely School (Hansard: Lords: 9th December 1998:1013), known for their involvement with the medical insurance industry and their liaison with policy-makers at the UK then-Department of Health, both of which institutions apparently preferring ME to be classified as a psychiatric, not a neurological, disorder, because mental disorders are excluded from medical insurance cover and qualify for reduced state benefits.

For almost 40 years, despite the fact that the WHO's International Classification of Diseases (ICD) has classified ME as a neurological disorder since 1969, those psychiatrists have "cancelled" ME by insisting that it doesn't exist except as a false belief, and that CFS is a psychiatric disorder. In 1994, psychiatrist Simon Wessely, self-appointed advisor to UK Departments of State (supported by contemporaneous correspondence), was categoric: he asserted that ME is *"simply a belief, the belief that one has an illness called ME"* and that it is *"part of the world of myth"* (Microbes, Mental Illness, the Media and ME: The Construction of Disease": Simon Wessely; 9th Eliot Slater Memorial Lecture, IOP, London 12th May 1994).

So certain was he that he was right, by working at the WHO Collaborating Centre for Mental Health at the Institute of Psychiatry, London, in 2000 he succeeded in re-classifying ME as a mental disorder without the knowledge or permission of the WHO Headquarters in Geneva. He was able to do this because, using the WHO logo, the Collaborating Centre produced a book ("Guide to Mental Health in Primary Care") which was based on Wessely's beliefs about ME. The Guide was funded by the UK Department of Health. Despite strenuous objections and despite WHO ICD classifications being mandatory in the UK, sales of the Guide were allowed to continue unabated until almost 30,000 copies had been sold, following which ME was classified as a mental disorder in the NHS Mental Health Data Manual. However, in September 2021 the WHO issued a statement repudiating the unofficial re-classification by the UK Collaborating Centre for Mental Health. The matter was raised in Parliament, where Earl Howe declared that Wessely had "*effectively hijacked the WHO logo to give credence to his own view of ME as a mental illness"* (Hansard: Lords: 23.01.04: vol 656: No.7: 1192).

Given Wessely's prodigious published output on ME/CFS – he himself numbers it to be 212 articles out of his total of over 1,000 published papers -- plus his numerous contributions to medical textbooks, his editorial control of journals including the BMJ, his relationship with the media, especially with the Science Media Centre (of which he was a founder member) which informs journalists including the BBC, his public appearances and pronouncements, it is hardly surprising that his doctrine permeates the UK medical fraternity, including the NHS, as well as other Departments of State. Despite the extensive published evidence that contradicts Wessely's dogma, it still prevails in the UK.

Since 1988 Wessely has publicly dismissed the substantive peer-reviewed evidence of the organicity of ME published since 1956, but an evidence-base of the published articles proving the organicity of ME does exist and is available at https://margaretwilliams.me/ and at https://www.oneagleswings.me.uk/margaretwilliams/

Although his work has been widely discredited in international scientific circles, Wessely has risen to become Regius Professor Sir Simon Wessely (the first Regius Professor of Psychiatry in the UK); he is the recipient of many accolades and honours including the highest civil honour in the land (GBE); he was appointed to the Judicial Appointments Commission (the body that selects and recommends candidates for judicial office in England and

Wales, a post he held for six years); he was appointed to NHS England and to the Board of the National Records and Archives, not forgetting his appointment as Fellow of the Royal Society. Without doubt he is one of the most influential people in the country.

None of these honours alters the fact that Wessely and his adherents have been proved wrong about the nature of ME/CFS. Many people believe they are accountable for immeasurable suffering by disseminating as factual information what has been disproved by scientific evidence, resulting in the denial of basic care and support to people with ME/CFS. It is believed by many people – both lay and professional, including GMC-registered physicians -- that the predominating influence of the Wessely School has resulted in unquantifiable iatrogenic harm (in some cases resulting in death, as confirmed by Coroners' Regulation 28 Notices) to extremely sick and vulnerable people and to their distressed relatives, harm that has been augmented by UK Social Services' widespread adherence to -- and imposition of – the Wessely School's dogma that ME is a psychosocial disorder with no organic pathology.

The 2025 Komaroff/Dantzer paper must surely obliterate the deeply damaging influence and control of these ill-informed mental health professionals. Regrettably, that appears not to be the case in the UK.

Whilst it is the case that the UK Government classifies ME/CFS as a neurological condition in compliance with the WHO, there is controversy about the name by which ME/CFS is now known in the UK. There has been a move to re-name it as a Functional Neurological Disorder (FND) by those who still believe it to be a mental disorder. A functional disorder is a condition where a bodily part or system does not work correctly even though standard tests show no abnormality. Labelling ME/CFS as a Functional Neurological Disorder creates a route for those with ME/CFS to be treated by mental health professionals, because in the medical world, functional disorders are widely known as NAD, which stands for "nothing abnormal discovered", so the patient is referred to a psychologist or psychiatrist for management. Patients with ME/CFS are being told that they have FND, so they think they have a "neurological" disorder, without realising that they have received a mental health diagnosis.

In its journal "ME Essential" Winter 2023, the ME Association published an explanation: "*…most neurologists don't now believe that ME (or CFS) is a neurological disease. In fact, in one published survey, the majority of UK neurologists (84%) said they did not believe that ME or CFS is a neurological disease and see it as a psychological problem…So diagnosing ME or CFS as a functional neurological disorder (FND) is the neurologists' way of describing patients who turn up in neurological clinics with neurological symptoms but not what they believe is a neurological disease. It's a similar form of diagnostic labelling to medically unexplained symptoms (MUS) or a functional somatic syndrome (FSS) that are used by other specialists who don't like the name ME. Neurologists don't normally want to get involved with the management of patients with FND…so they may refer the patient to a psychologist or psychiatrist for management".*

This explanation contrasts with what St George's Hospital, London, states about its FND clinic, which is that ME/CFS is **not** treated there**:** their published exclusion criteria explicitly list "chronic fatigue" as a reason for non-referral. This presents another anomaly, because "chronic fatigue" is **not** the same disorder as "chronic fatigue syndrome/CFS". However, whilst St George's states that ME/CFS sits outside its FND diagnostic framework, it is notable that a "Multidisciplinary Symposium in Functional Disorders" is scheduled to take place on 11th September 2026 at the Tooting Campus of CITY St George's University of London. It is expressly stated that ME/CFS is **not** on the agenda and is not included as a topic. It is therefore notable that the speakers' topics include what might rationally be described as the Wessely School's well-documented perception of people with ME/CFS. Professor Trudie Chalder (a long-time ardent member of the Wessely School) will be speaking on *"A trans-diagnostic cognitive behavioural treatment for persistent physical symptoms"*. Other subjects are *"Health-related anxiety"* (to be given by Professor Jon Stone, described as a leading neurologist who specialises in FND and a long-time published supporter of the Wessely School's beliefs)*; Occupational Therapy for Functional Neurological Disorder"* and *"Malingering, feigning and exaggeration"* (to be given by Professor Mark Edwards, a neurologist at St George's who specialises in FND).

One can but wonder if this is not a master-class in subterfuge, especially bearing in mind that Trudie Chalder is on record (preserved on video) stating: *"I mean I think it's important to incorporate that belief in a more sophisticated model of understanding the illness than you would share with the patient…. people think that there's something lurking in the cupboard as yet undiscovered that is creating the problem and of course that's, I think…a*

bit silly. It's really important that patients keep a detailed diary of their activities so that you can then re-order all of the activities" (the Wessely School's 2002 "Training Physicians in Mental Health Skills").

Undoubtedly, the Wessely School's management of ME/CFS patients remains operative in the UK: very recently, the mother of a young woman with severe ME was arrested for trying to protect her sick daughter from being forced to undergo an intervention favoured by the Wessely School, an intervention that is now forbidden by the NICE Guidelines 2021 (NG 206) because it has been proved to be harmful and has no scientific basis. Without doubt, Wessely School adherents do not accept -- and refuse to comply with -- the revised NICE Guidelines, as evidenced by their published response co-signed by 49 supporters (White P et al. JNNP 2023:94:1053-1063).

What follows is taken from the Komaroff/Dantzer Review.

Extracts taken from the Komaroff/Dantzer Review of the Causes of Symptoms and Symptom Persistence in long COVID and ME/CFS

"Many similar underlying biological abnormalities have been identified in both conditions, including autoantibodies against neural targets, endothelial dysfunction, acquired mitochondrial dysfunction, and a pro-inflammatory gut microbiome. Each of these abnormalities may directly cause some of the symptoms. In addition, symptoms may be caused by ancient metabolic responses to vital threats (sickness behaviour) mediated by recently discovered neural circuits; these circuits constitute a symptom-generating pathway, activated by neuroinflammation. Many factors cause the symptoms to become chronic, including the fact that many of the underlying biological abnormalities reinforce each other, creating physiological vicious cycles."

"Many health professionals have regarded both illnesses as rare and have even doubted that the symptoms were caused by objective biological abnormalities. It is now clear that neither is the case."

"Underlying abnormalities in ME/CFS and Long COVID"

"Neurological/neuromuscular abnormalities"

"neuroinflammation; autonomic dysfunction; reduced cerebral blood flow; cognitive deficits; autoantibodies against neuronal targets in the central and autonomic nervous system; hypocortisolism; increased oxidative stress; small fibre neuropathy; gray and white matter abnormalities; pain and sensory abnormalities; impaired connectivity between brain regions; brainstem dysfunction; plasma and cerebrospinal fluid markers of neural injury; sleep disorders; exercising muscle displays redox imbalance and impaired mitochondrial function; tryptophan pathway abnormalities; circadian dysregulation".

"Immunologic/infectious abnormalities"

"persisting viral reservoirs/tissue injury/reactivation of latent virus; pro-inflammatory gut microbiome; NK cell dysfunction; systemic inflammation, with elevated numbers of pro-inflammatory cytokines that correlate with severity of symptoms; increased numbers of activated CD8+ cytotoxic T cells; T cell exhaustion in long-term illness; B cell abnormalities; increased levels of autoantibodies; activation of the complement system; increased apoptosis of various white cells; mast cell activation syndrome; accelerated cellular senescence".

"Metabolic abnormalities"

"redox imbalance; increased levels of pro-oxidants; decreased levels of anti-oxidants; increased nitrosative stress; reduced generation of ATP; a systemic hypometabolic state – reduced levels of multiple metabolites; reduced levels of cortisol secondary to down-regulation of the HPA axis; tryptophan pathway abnormalities including impaired absorption (in long Covid) and polymorphisms and autoantibodies that correlate with symptom severity (in ME/CFS)."

"Cardiovascular/pulmonary abnormalities"

"endothelial dysfunction; blood-brain barrier disruption that correlates with cognitive deficits; reduced peak VO2 (diminished exercise capacity); increased VE/VCO2 slope (reduced ventilatory efficiency); reduced preload (venous return to the right heart); platelet abnormalities/coagulopathies; increased von Willebrand factor ratio (*defined elsewhere as a large blood protein which acts like a glue to help blood clot*), creating a prothrombotic state and activating complement."

The authors refer to the preponderance of published evidence from different laboratories supporting these abnormalities

"Genetic vulnerabilities"

"A recent whole-genome sequencing study identified 115 risk genes for ME/CFS (and) specific gene expression patterns correlated with specific groups of symptoms. The involved genes implicate the central nervous system and the immune system in the pathology of the illness. An analysis that correlates combinations of polymorphisms with long Covid and ME/CFS found robust associations (findings confirmed in a second large population). The genes involved have previously been linked to neurological and cardiometabolic diseases."

"Some abnormalities can directly cause symptoms"

"Several of the underlying biological abnormalities can directly cause some of the symptoms. For example, autonomic dysfunction that leads to reduced cerebral blood flow can impair cognitive performance (and) endothelial dysfunction can cause vascular spasm and coagulopathy that, together, reduce blood flow and disrupt the blood-brain barrier, both of which could directly impair cognitive performance. Endothelial dysfunction and fibrin may indirectly cause symptoms by stimulating neuroinflammation. Autoantibodies against neural targets could cause symptoms; trained immunity could stimulate systemic inflammation – a phenomenon in which innate immune cells acquire a non-specific memory of a past infection that results in an aberrant and excessive activation of various innate immune pathways following a new infection, even if the new infection is with a different agent from the one that initially triggered the hyperresponsive state."

"The purpose of sickness symptoms and behaviour"

"Sickness behaviour (*defined elsewhere as a combination of lethargy, fatigue, somnolence, anorexia, social withdrawal, hyperalgesia, anhedonia and cognitive disturbance*) reduces the consumption of ATP, thereby reserving the ATP needed to support the most essential vital activities, as well as to fuel the inflammatory responses needed to fight the infection and to heal tissue injury."

"Neuroinflammation"

"Neuroinflammation triggers sickness symptoms and brain hypometabolism; (it) generates a hypometabolic state in the brain, particularly in the cortex and hippocampus, as well as a persisting disruption of the blood brain barrier. The mechanism by which inflammation affects fatigue and mood is being revealed: several studies have identified pro-inflammatory and anti-inflammatory cytokines, cytokine receptors on neural cells and specific types of neurons and neural circuits involved in the much-reduced ability to exert oneself."

"Neuroinflammation can be triggered from inside and outside the brain"

"Neuroinflammation – activation of the brain's innate immune system – plays a central role in generating sickness symptoms. One potential trigger of neuroinflammation is active infection (new or reactivated) of the brain.

Another is the need to repair brain injury caused by a previous infection, even if the infectious agent and/or its molecular residue may no longer be present. In addition, it has become clear that inflammation outside the brain can also trigger neuroinflammation. The response of the immune system to microbial pathogens does not stay local: it propagates to the brain through humoral and neural pathways. The peripheral inflammatory molecules that generate humoral and neural signals to the brain include cytokines, prostaglandins and activated complement factors, which activate the brain's innate immune system. Thus, an inflammatory process anywhere in the body – such as in the lungs or gut -- can generate neuroinflammation and, hence, sickness symptoms. Neuroinflammation --whether due to an inflammatory stimulus inside the brain or peripheral inflammation relayed to the brain -- appears necessary to initiate sickness symptoms."

"The reduced generation of ATP"

"People with both long COVID and ME/CFS have a reduced capacity to generate ATP from oxygen, glucose, fatty acids and amino acids. Energy generation does not rise to compensate for the ATP consumed – indeed, it is reduced."

"Mitochondrial injury"

"Infection, particularly persistent infection, can impair mitochondrial function (which) can emphasise anaerobic glycolysis, likely driving the increases in lactic acid levels which have been reported in these illnesses. In addition, intracellular infection can drive aerobic glycolysis, leading to inefficient production of ATP from glucose. Mitochondrial stress responses increase whole-body energy demand, and stress responses in one tissue or organ can initiate mitochondrial dysfunction in multiple organs."

"Underlying abnormalities that can reinforce each other and cause persisting vicious cycles of pathology and symptoms"

"Reinforcing abnormalities"

"mitochondrial injury and inflammation; inflammation generates ROS that can induce mitochondrial injury, requiring not only the generation of new mitochondria but also the elimination of the damaged mitochondria; reduced levels of ATP (lead) to further decreases in energy production and further increases in inflammation and oxidative stress – a vicious cycle"

"mitochondrial injury and persisting infection; mitochondrial dysfunction of leukocytes can impair the immune response to infection because mitochondria modulate both adaptive and innate immune responses. Failure to eradicate infection increases mitochondrial injury – a vicious cycle"

"redox imbalance and energy production; ROSs damage mitochondria DNA and proteins, causing a decrease in ATP production; damaged mitochondria release DNA fragments, activating toll-like receptor (TLR) signalling, perpetuating inflammation, increased ROS, and reduced energy production – a vicious cycle"

"redox imbalance and endothelial dysfunction; redox imbalance enhances senescence of endothelial cells and encourages endothelial dysfunction which, in turn, generates local redox imbalance – a vicious cycle"

"endothelial dysfunction, NK cell dysfunction and neuroinflammation; neuroinflammation and endothelial injury both produce ROS that encourages further neuroinflammation and endothelial dysfunction – a vicious cycle. NK cell dysfunction encourages viral activation and replication, which elicits a further inflammatory response, encouraging further neuroinflammation and endothelial dysfunction – a vicious cycle"

"dysautonomia and inflammation; the ANS is in constant bidirectional communication with the immune system. Autonomic *afferents* signal the brain after detecting inflammation through pattern recognition receptors such as TLRs, cytokine receptors and prostaglandin receptors. In turn, the ANS sends *efferent* signals to the immune

system that can be both pro-inflammatory and anti-inflammatory; thus, dysautonomia triggered by neuroinflammation could impair the body's ability to contain inflammation – a vicious cycle"

"dysautonomia and gut microbiome dysbiosis; gut dysmotility resulting from dysautonomia can lead to small intestinal bacterial overgrowth (SIBO) and dysbiosis of the gut microbiome, which, in turn, can generate neuroinflammation, leading to dysautonomia – a vicious cycle"

"redox imbalance and NK cell dysfunction; NK cell dysfunction encourages viral reactivation and replication, resulting in inflammation and redox imbalance, which, in turn, can impair NK cell function – a vicious cycle"

"peripheral inflammation triggers neuroinflammation and vice versa; peripheral inflammation triggers neuroinflammation through humoral and neural pathways and neuroinflammation can upregulate and activate transcription pathways in peripheral organs such as skeletal muscle – a vicious cycle."

"There is little evidence that a *single, novel* infectious agent causes ME/CFS. Instead, it is likely that ME/CFS can be triggered by *multiple, different* infectious agents."

"Persistence of injury requiring repair through an inflammatory response"

"Even if the virus and its component molecules are no longer present, the tissue injury caused by the infectious agent can persist, eliciting an ongoing inflammatory response. This includes persistent injury in the brain. Recently it has been shown that endothelial injury and associated coagulopathy – in addition to reducing blood flow in the microcirculation – can also produce pro-inflammatory clots that drive ongoing thrombo-inflammation, redox imbalance, neuroinflammation and neuronal loss in mice infected with SARS-CoV-2 (and) similar circulating micro-clots have been noted in ME/CFS as well as long COVID."

"Defective recovery from inflammation"

"Recovery from inflammation triggered by the presence of an infectious agent, or the need to heal tissue injury, is mediated by various chemosensory receptors that are part of the cell danger response and can be interrupted, leading to persistent inflammation."

"Reactivation of latent infectious agents, particularly herpesviruses"

"Reactivation of latent infectious agents occurs in both long COVID and ME/CFS. Reactivation of viruses other than herpesviruses as well as bacteria also has been documented. Peripheral reactivation would be sufficient to generate the humoral and retrograde neural signals that can trigger neuroinflammation. There is also evidence that herpesviruses are capable of infecting and achieving latency in endothelial cells, possibly triggering and perpetuating endothelial dysfunction, which is seen in both long COVID and ME/CFS."

"Dysbiosis of the gut microbiome"

"Dysbiosis of the gut microbiome, leading to a state of low-level inflammation, has been documented in both long COVID and ME/CFS. This local inflammatory state causes breaches of the gut-blood barrier, with leakage into the circulation of not only inflammatory molecules but also bacterial and fungal products. This "leaky gut" is a plausible cause of chronic systemic inflammation."

"Autoimmunity"

"Hundreds of autoantibodies are generated during acute COVID 19. A recent study of 55 people with long COVID with neurological symptoms found that many had autoantibodies directed at human and rodent neural antigens

and that specific autoantibodies correlated with particular symptoms. Many autoantibodies have been identified in ME/CFS."

"Abnormalities that reinforce each other, creating vicious cycles that perpetuate the pathology"

"Of particular importance (is that) many of the underlying abnormalities in people with long COVID or ME/CFS have bidirectional connections (so) there is the potential for an ongoing vicious cycle that perpetuates the abnormalities and the symptoms the abnormalities cause. It is likely that the predominant abnormalities in one individual may differ from those in another individual."

"CONCLUSIONS AND FUTURE DIRECTIONS"

"Globally, long COVID and ME/CFS are causing hundreds of millions of people to suffer and are costing society hundreds of billions of dollars. Initially it was not clear if there were any underlying biological abnormalities that could explain the symptoms of the two illnesses. It is now clear that there are, and that the two illnesses share a complex underlying pathophysiology. We address the question of how the multiple underlying abnormalities found in these illnesses may be causing both the symptoms and the chronicity of the symptoms. Each abnormality can directly cause some of the symptoms. Discovering which is predominant in any individual with these illnesses will not be easy. The central focus of this review is to propose an additional cause of the symptoms, one that can be triggered by the underlying abnormalities and that might be more easily targeted for therapy."

"Implications for treatment"

"There is no evidence that targeting any single, specific abnormality – for example, dysautonomia, autoantibodies to neural targets, and residual tissue reservoirs of virus – cures the symptoms in all people. We propose another target for therapy: the neuroinflammation that activates the neural circuits that may generate the sickness symptoms – including fatigue, brain fog and pain. Targeting neuroinflammation may reduce many of the symptoms of these illnesses. However, experience suggests that traditional anti-inflammatory drugs are unlikely to be effective and that new therapies will be required. The deepening understanding of the underlying pathophysiology should lead to effective new therapies for the people whose lives have been interrupted and diminished by these illnesses."

The authors provide 204 references.