The role of viruses in ME/CFS: what, if any, will be the effect of the discovery linking XMRV to ME/CFS on the MRC PACE Trial?

Margaret Williams **21st November 2009**

For decades it has been known and shown that viruses play a role in ME/CFS; some illustrations from the literature are provided below (all of which are relevant and significant).

In relation to "CFS", the most-studied viruses have been the Epstein-Barr Virus (EBV) and the Human Herpes Virus-6 (HHV-6). In relation to "pure" ME, the most studied viruses (and for which there is extensive evidence) have been the enteroviruses, usually Coxsackie B (CBV). Some illustrations from the literature of the role that viruses play in ME/CFS are provided at the end of this paper; all are significant.

There is increasing awareness that the dysregulated immune system that is a hall-mark of ME/CFS allows multiple latent viruses and microbial agents to become reactivated (Co-Cure NOT:12th November 2009).

Moreover, recent research has shown that even viruses which were hitherto believed not to persist after an acute infectious episode are capable of long-term viral persistence.

Nora Chapman et al from the Enterovirus Research Laboratory, Department of Pathology and Microbiology, University of Nebraska Medical Centre, have shown that human enteroviruses Coxsackie B can naturally delete sequence from the 5' end of the RNA genome and that this deletional mechanism results in long-term viral persistence, which has substantially altered the previously held view (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2440640/?tool=pubmed). In a specially commissioned piece for the charity Invest in ME, the researchers say: "*This previously unknown and unsuspected aspect of enterovirus replication provides an explanation for reports of enteroviral RNA detected in diseased tissue in the apparent absence of virus particles"* (Journal of IiME 2009:3:1).

Dr John Chia, an infectious diseases specialist from Torrance, California, who specialises in ME/CFS, is on record: "*I believe that the main reason (ME)CFS patients are symptomatic is due to continuing inflammatory response toward viruses living within the cells, enteroviruses in most of the cases I see. We have clearly documented certain enterovirus infections triggering autoimmune responses in some patients…**Can you imagine how we would feel if there are viruses surviving in our muscles, brains, hearts and gastrointestinal tracts triggering ongoing immune responses?"*** (http://aboutmecfs.org/blog/?p=865).

The CFIDS Chronicle (Research Update, Summer 1993) explained viruses and retroviruses as follows:

"*A virus is a microscopic organism that lives within the cells of another living organism. Viruses cause disease at the most basic level, by damaging the cells of living things. By themselves, viruses are lifeless particles incapable of reproduction, but once they enter the cell of another living thing they become active organisms that can multiply hundreds of times.*

"Viruses are comprised of two parts – a core of either deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) and a protective envelope of protein. RNA viruses are smaller than DNA viruses and sometimes contain a special enzyme called reverse transcriptase which allows them to convert RNA to DNA. These specialised viruses are known as retroviruses and have a unique ability to merge with the host's own genetic material.

"Retroviruses have the unique ability to replicate themselves by (i) making a double-stranded DNA copy called a 'pro-virus' once they enter living cells. Pro-viruses integrate themselves into the human chromosome and become part of the host's genetic code (ii) alter the host's immune response by evading detection as a 'hidden invader' (iii) remain hidden and latent, spliced within the host's DNA, for long periods of time. Retroviruses are known to be potent stimulators of cytokines".

On 8th October 2009 the premier journal Science published a paper online showing a direct link between a retrovirus and ME/CFS (Detection of infectious retrovirus XMRV, in blood cells of patients with chronic fatigue syndrome. Lombardi VC, Ruscetti FW, Peterson DL, Silverman RH, Mikovits JA et al) which caused global reverberations.

However, this was not the first time that a retrovirus had been associated with ME/CFS.

In 1991, using polymerase chain reaction and in situ hybridisation, Dr Elaine De Freitas, a virologist at the Wistar Institute, Philadelphia (which is America's oldest independent institution devoted to biological research) and Drs Daniel Peterson, Paul Cheney, David Bell et al found such an association (Retroviral sequences related to human T-lymphotropic virus type II in patients with chronic fatigue immune dysfunction syndrome. Proc Natl Acad Sci USA 1991:88:2922-2926). It is notable that co-author Hilary Koprowski is a distinguished virologist and Professor Laureate who was Director of the Wistar Institute from 1957-1991; he is a member of the US National Academy of Sciences and is Director of the Centre for Neurovirology at Thomas Jefferson University.

Before publication, the findings were presented on 4th September 1990 by Elaine De Freitas at the 11th International Congress of Neuropathology in Kyoto, Japan.

Ten days later, on 14th September 1990 Dr Peter White (as he then was) and other members of the Wessely School dismissed the findings: *"in the vast majority of CFS cases there is a psychological component. About 75% of CFS sufferers are clinically depressed, according to Peter White, senior lecturer in the department of psychiatric medicine at St Bartholomew's Hospital in London.* ***White said he believes depression is often a cause, rather than a consequence, of CFS****…****Les Borysiewicz, a clinical virologist at Addenbrookes Hospital in Cambridge*** (now Chief Executive of the MRC, having succeeded Professor Colin Blakemore) ***(said) 'Whatever causes CFS, it isn't the virus itself'****…Anthony Clare, psychiatrist and medical director of St Patrick's Hospital in Dublin* (now deceased), *pointed out that…there have been many 'fatigue' diseases with shifting causes: 'Neurasthenia, food allergies, now viruses. Some people would always rather have a disease that might kill them than a syndrome they have to live with' "* (Science 1990:249:4974:1240).

In their PNAS article that was published in April 1991, De Freitas et al noted that chronic fatigue immune dysfunction syndrome (CFIDS) *"may be related or identical to myalgic encephalomyelitis"* and examined adult and paediatric CFIDS patients for evidence of human retroviruses (HTLV types I and II). As the CFIDS Chronicle article noted, the Wistar team looked at the peripheral blood DNA to see if they could find messenger RNA (mRNA) encoding for a viral segment of the HTLV-II virus.

At that time, known human retroviruses were the human immunodeficiency viruses 1 and 2 (HIV-1 and HIV-2) which are known to cause AIDS, and human T-lymphotropic viruses HTLV-I which causes lymphoma and HTLV-II which causes leukaemia (Hunter-Hopkins ME-Letter, October 2009). The four segments of the HTLV-II virus are referred to as the *env*, *gag*, *pol* and *tax.*

After a two year study, De Freitas et al provided evidence for HTLV-II-like infection of blood cells from CFIDS patients (and also to a lesser extent from people closely associated with them). This evidence was further substantiated by patient reactivity to proteins with the molecular weights reported for HTLV-I and HTLV-II antigens.

In their article, De Freitas et al said: "*The frequency of these antibodies in CFIDS patients compared with healthy non-contact controls suggests exposure / infection with an HTLV-like agent rare in healthy non-contact people".*

Whilst none of the CFIDS patients' blood sample contained detectable HTLV-I gag sequences, DNA from at least two separate bleedings was positive for the HTLV-II gag subregion in 83% of adult and 72% of paediatric CFIDS patients, and the authors pointed out that *"similar frequencies of PBMCs* (peripheral blood mononuclear cells) *expressing retroviral mRNA have been reported for HIV-infected individuals…The clinical*

histories of these CFIDS patients do not reveal behavioural or genetic factors usually associated with retroviral infection. Yet our data suggest that not only are these HTLV-II-like genes and HTLV-reactive antibodies associated with CFIDS in patients but that samples from a significant proportion of their non-sexual contacts are positive".

De Freitas et al were careful to emphasise that "*Although our data support an association between an HTLV-like agent and CFIDS, we cannot, as yet, define the agent's role in the disease process. It may be a secondary infection to which immunologically compromised patients are susceptible. Alternatively, it may be one of two viruses that, when co-infecting the same haematopoetic cells, induce immune dysfunction".*

Following the Wistar findings, researchers at the US Centres for Disease Control (CDC) allegedly attempted to replicate De Freitas' work but failed to do so; this was suggested to be because certain scientists appeared eager to discount any possibility of a retroviral association with CFIDS. De Freitas defended her work and insisted that the CDC investigators had modified her assays, with the result that her work could not be replicated by the CDC.

De Freitas was publicly discredited; her research funding was discontinued and her research abandoned; she was subjected to what appeared to be attempts to destroy her professional reputation. Commenting on the subsequent discovery of XMRV (see below), ME/CFS expert Dr Paul Cheney of The Cheney Clinic was unambiguous: "*Her work was unfortunately assaulted by the CDC. Her proposal to fly to the CDC in Atlanta to physically run the assays side by side with the CDC scientists was dismissed by the CDC"* (http://cheneyclinic.com/a-retrovirus-called-xmrv-is-linked-to-cfs/538).

In August 1991, together with co-author Brendan Hilliard, Elaine De Freitas had applied for a world patent that was subsequently issued in April 1992. Detailed information has been provided by Dr Alan Cocchetto, Medical Director of The National CFIDS Association (http://www.ncf-net.org/forum/revelations.html). Cocchetto is clear: "*the contents of this paper have major implications due to the depth and scientific quality of the work…The entire patent is approximately 40 pages. If the NIH ignored the depth of this work… then the NIH dropped the ball on this one and should be held accountable.* ***The inventors even state: 'The ability to screen blood samples infected by CAV* (CFIDS-associated virus) *enables producers and distributors of blood products, eg. the American Red Cross, to identify and discard donated blood…intended for use in transfusions…If unscreened, the use of such blood and blood-derived products could contribute to the spread of CFIDS'***. *The inventors reveal: 'Neither HTLV-I, II, nor HIV virions have ever been found inside mitochondria…****the positive results support the possibility that this CAV is capable of casual transmission to non-infected persons'.*** *If the NIH ignored this last comment, then something is dramatically wrong with the agency that is supposed to protect and safeguard the welfare of the citizens of the United States.* ***Again, the implications here are just staggering****…The only conclusion that can be reached is that this work is very thorough and extensive. It has been funded by the NIH….Any retrovirus that can invade the mitochondria directly indicates trouble. As far as I'm concerned, there needs to be a criminal investigation of the NIH regarding why they refused to fund upon submission of all this data".*

It has been said that De Freitas's reputation was intentionally destroyed because her research did not support the theory that (ME)CFS is a psychoneurosis, and that her public discrediting caused others to fear following up her work (Co-Cure;NOT: 16th October 2009).

As Neenyah Ostrom commented: "*CFS and AIDS do not exist primarily in a scientific environment: they exist, for the most part, in an extremely political environment"* (New York Native, 28th November 1994).

There undoubtedly seems to be collaboration about policy concerning ME/CFS between the UK Wessely School and Dr William (Bill) Reeves, Principal Investigator of the CDC's CFS research programme, who is held in the same disregard in the US as Professor Simon Wessely is held in the UK (see below).

Regarding blood donation by people with ME/CFS, it is a matter of record that in reply to a letter dated 21st December 1991 from the late Joan Irvine, on 16th January 1992 Dr George Rutherford, Chief of the Infectious

Diseases Branch of the US Department of Health and Human Services, replied to her query about blood donation by people with (ME)CFS:

"…a number of researchers have postulated that it may be caused by an infectious agent or agents, such as a virus…Based on our knowledge of infectious diseases of the immune system, it is not impossible that one or more of these suggested agents might potentially be able to be transmitted through blood-to-blood contact, as occurs in blood transfusions…I think that it is best to await further research findings before resuming blood donation".

Also on 16th January 1992, the same Dr William Reeves of the CDC wrote to Joan Irvine about the same issue:

"…since on-going research indicates an infectious agent may be involved in some cases of CFS it would seem prudent to refrain from donating blood until this issue is resolved" (http://www.cfs-news.org/joan.htm).

It is worth noting that people in the UK with ME have been **permanently** excluded from donating blood since at least 1989 (Guidelines for the Blood Transfusion Service in the UK, 1989: 5.4; 5.42; 5.43; 5.44; 5.410).

This was subsequently upheld by the Parliamentary Under Secretary of State The Lord Warner, who confirmed in writing on 11th February 2004 in a letter to the Countess of Mar that people with ME/CFS are not permitted to be blood donors. Lord Warner was unambiguous: *"We have checked with the National Blood Service and they have provided the following information. The NBS guidelines on donor selection on ME refer to those on Post Viral Fatigue Syndrome. The Guidance is: defer from blood donation until recovery. The underlying logic is that this condition is possibly viral and therefore the NBS cannot accept the risk of possible transmission by blood. Since the condition is very variable and sometimes prolonged, it could become a lifetime ban in any particular case. I have copied this letter to the House (of Lords) library".*

Given the (re)-discovery of a direct link between a retrovirus and ME/CFS, the importance of this cannot be over-stated.

Notably, those with a behavioural disorder are not prevented from donating blood.

XMRV (retrovirus associated with ME/CFS)

As mentioned above, in October 2009 the journal Science published a paper by collaborators from the Whittemore Peterson Institute, the US National Cancer Institute and The Cleveland Clinic that demonstrated a direct link between the retrovirus XMRV and ME/CFS (Science: 8th October 2009:10.1126/science.1179052).

XMRV stands for xenotropic murine leukaemia virus-related virus (xenotropic meaning a virus that can grow in the cells of a species foreign to the normal host species, ie. a virus that is capable of growing in a foreign environment).

XMRV is a member of the same family of retroviruses as the AIDS virus. A retrovirus inserts itself into the host's genetic material by copying its genetic code into the DNA of the host by using RNA and once there, it stays for the life of the host.

It is understood that Mikovits' discovery was deemed to be of such magnitude by the world's most prestigious science journal that the authors' paper (which was submitted on 6th May 2009) was sent to three times the customary number of referees prior to acceptance and publication.

Shortly before the Mikovits et al paper was published, on 24th September 2009 the Whittemore Peterson Institute (WPI) announced that Dr Mikovits and collaborator Dr Jonathan Kerr of St George's, London, had

been awarded a $1.6 million five-year grant by the US National Institute of Allergy and Infectious Diseases for research into the causes and diagnosis of neuro-immune diseases (http://www.wpinstitute.org/news/news_current.html). The Project Number is 1R01A1078234-01A2 and the description provided by the applicants says:

"CFS is a complex disease estimated to affect between 0.5% - 2% of the population of the Western world. ***Its pathogenesis is thought to involve both inherited and environmental (including viral) components, as with other chronic inflammatory diseases such as multiple sclerosis…Consistent with this chronic inflammatory context, CFS patients are known to have a shortened life-span and are at risk for developing lymphoma.*** *We hypothesise that chronic inflammatory stimulation from active and recurrent infections of multiple viruses on a susceptible host genetic background leads to the pathogenesis characterised by CFS. The overall goal of this research project is to define those viral and host parameters…The proposed research will provide significant insight into the disease mechanism of Chronic Fatigue Syndrome so accurate testing and specific treatments can be developed with a goal of curing the disease and preventing life-threatening complications"* (Co-Cure NOT:RES:21st October 2009).

It is worth noting that three days before the Mikovits et al article was published in Science, on 5th October 2009 Professor Peter White in collaboration with Dr Bill Reeves of the CDC published a paper in which they described endophenotypes of CFS (which White talked about in his presentation at Bergen on 20th October 2009 – see below). According to Wikipedia, "endophenotype" is a psychiatric concept, the purpose of which is to divide behavioural symptoms into separate phenotypes with clear genetic connections. The relevance of this to the neuro-immune disease ME/CFS has not been explained, but White and Reeves et al concluded: *"The data do not support the current perception that CFS represents a unique homogeneous disease"* (Population Health Metrics 2009:7:17doi:10.1186/1478-7954-7-17).

In contrast, in their article in Science Mikovits et al deal with science, not speculation:

"Chronic fatigue syndrome (CFS) is a debilitating disease of unknown aetiology that is estimated to affect 17 million people worldwide.

"Studying peripheral blood mononuclear cells (PBMCs) from CFS patients, we identified DNA from a human gammaretrovirus (XMRV) in 68 of 101 patient (67%) compared to 8 of 218 (3.7%) healthy controls" (gammaretroviruses are known to cause cancer, immunological and neurological diseases in animals).

"Cell culture experiments revealed that patient-derived XMRV is infectious and that both cell-associated and cell-free transmission of the virus are possible".

"CFS affects multiple organ systems in the body. Patients with CFS display abnormalities in immune system function, often including chronic activation of the innate immune system and a deficiency in natural killer (NK) cell activity. A number of viruses, including ubiquitous herpesviruses and enteroviruses have been implicated as possible environmental triggers of CFS. Patients with CFS often have active β herpesevirus infections, suggesting an underlying immune deficiency.

"The recent discovery of a gammaretrovirus, XMRV, in the tumour tissue of a subset of prostate cancer patients prompted us to test whether XMRV might be associated with CFS. Both of these disorders, XMRV-positive prostate cancer and CFS, have been linked to alterations in the antiviral enzyme RNase L" (RNase L is the terminal enzyme in the 2-5A synthetase/RNase L antiviral pathway in the immune system and it plays an essential role in the elimination of viral mRNA. Deregulation of this pathway in subsets of ME/CFS patients has been reported extensively in the scientific literature. In ME/CFS, a wide spectrum of cleavage of RNase L is observed, a phenomenon also seen in MS patients, and such altered RNase L activity profoundly affects cellular physiology, including apoptosis or programmed cell death – Dr Neil Abbot: Co-Cure RES:MED: 16th October 2009).

"Neurological maladies and immune dysfunction with inflammatory cytokine and chemokine up-regulation are some of the most commonly reported features associated with CFS…The presence of infectious XMRV in lymphocytes may account for some of these observations of altered immune responsiveness and neurological function in CFS patients.

"In summary, we have discovered a highly significant association between the XMRV retrovirus and CFS.

"This observation raises several important questions. Is XMRV infection a causal factor in the pathogenesis of CFS or a passenger virus in the immunosuppressed CFS patient population?…Conceivably these viruses could be co-factors in pathogenesis, as is the case for HIV-mediated disease, where co-infecting pathogens play an important role. Patients with CFS have an elevated risk of cancer.

"It is worth noting that 3.7% of the healthy donors in our study tested positive for XMRV sequences. This suggests that several million Americans may be infected with a retrovirus of as yet unknown pathogenic potential".

The published supplementary material confirms: "*Banked samples were selected for this study from patients fulfilling the 1994 CDC Fukuda Criteria for Chronic Fatigue Syndrome and the 2003 Canadian Consensus Criteria for Chronic fatigue syndrome / myalgic encephalomyelitis and presenting with severe disability".*

Commenting on this discovery, Professor John Coffin from the Department of Molecular Microbiology, Tufts University, Boston, a National Academy of Science member and expert retrovirologist who edited the 1997 reference book "Retroviruses" (proclaimed as "outstanding" by the New England Journal of Medicine) who was not involved with the study and who was at first highly sceptical but who was converted by the WPI team's independent lines of evidence, together with Professor Jonathan Stoye from the UK National Institute for Medical Research, Mill Hill, London (who is Head of the Virology Division at the Medical Research Council), stated:

"*Although chronic inflammation is often found in these patients, no infectious or toxic agent has been clearly implicated in this disease….Chronic fatigue syndrome is not the first human disease to which XMRV has been linked. The virus was first described about three years ago in a few prostate cancer patients and recently detected in nearly a quarter of all prostate cancer biopsies. It has been isolated from both prostate cancer and chronic fatigue syndrome patients, and is similar to a group of endogenous murine leukaemia viruses (MLVs)…There is more than 90% DNA sequence identity between XMRV and xenotropic MLV, and their biological properties are virtually indistinguishable.*

"There are several lines of evidence that transmission happened in the outside world and was not a laboratory contaminant. One is that XMRVs from disparate locations and from both chronic fatigue syndome and prostate cancer patients are nearly identical…Other evidence includes the presence of XMRV and high amounts of antibodies to XMRV and other MLVs in chronic fatigue syndrome and prostate cancer patients.

"Two characteristics of XMRV are particularly noteworthy. One is the near genetic identity of isolates from different diseases and from individuals in different parts of the United States. The two most distantly related genomes sequenced to date differ by fewer than 30 out of about 8,000 nucleotides. Thus, all of the XMRV isolates are more similar to each other than are the genomes isolated from any one individual infected with the human immunodeficiency virus.

"Another notable feature of XMRV is that the frequency of infection in nondiseased controls is remarkably high.

"If these figures are borne out in larger studies, it would mean that perhaps 10 million people in the United States and hundreds of millions worldwide are infected with a virus whose pathogenic potential for humans is still unknown" (www.sciencexpress.org/8th October 2009/Page 2/10.1126/science.1181349).

Announcing their groundbreaking discovery, a press release by R&R Partners on behalf of the Whittemore Peterson Institute said: "***Since the original Science paper was submitted, we have continued to refine our test for XMRV and have surprisingly found that 95% ME/CFS samples tested positive for XMRV antibodies in the plasma. 'This finding clearly points to the retrovirus as a significant contributing factor in this***

illness' *said Judy Mikovits, director of research for WPI.* ***This landmark study was the first to isolate XMRV particles from the blood and show that it can be transmitted between blood cells. Researchers have confirmed that this retrovirus is transmitted through body fluids and is not airborne"*** (http://www.wpinstitute.org/xmrv/docs/wpi_pressrel_100809.pdf).

Commenting on this further information, ME/CFS expert Dr Paul Cheney said: "***The finding of antibody or active virus in 95% of CFS and 4% of controls is a result that argues for causality, in my opinion….This retrovirus could easily …induce all manner of pathogens as seen in CFS (and) could corrupt the gut ecology …observed in CFS and lead to environmental illness as well. Time will tell, but I think Dr Mikovits is right to suspect causality***" (http://cheneyclinic.com/a-retrovirus-called-xmrv-is-linked-to-cfs/583).

On the day that the news broke of the XMRV link with ME/CFS, it was widely reported; prominent sources included AFP; Reuters; Wall Street Journal; Washington Post; New York Times; Nature; Scientific American; New Scientist; NIH News; Science News; NCI Press Release; Scientist, and many national newspapers such as the UK's Daily Telegraph and The Independent. Numerous links can be found at http://bit.ly/13nShx .

The Wall Street Journal quoted Judy Mikovits as saying that the XMRV virus creates an underlying immune deficiency which might make people vulnerable to a range of diseases, and it continued: *"Although Thursday's scientific paper doesn't demonstrate conclusively that XMRV is the cause of CFS, additional unpublished data make it a very strong possibility…****'Just like you cannot have AIDS without HIV, I believe you won't be able to find a case of CFS without XMRV' Dr Mikovits said****. …Dr Mikovits also said they also found XMRV in people with autism, atypical multiple sclerosis and fibromyalgia…Robert Silverman, a professor at the Cleveland Clinic Lerner Research Institute who is one of the co-authors of the study and one of the discoverers of the XMRV virus, said 'in most cases, people's immune systems are probably able to control the virus'….Researchers are already starting to test anti-retroviral therapies developed for AIDS to see if they are effective against XMRV".*

AFP (Agence France Presse) quoted Mikovit's co-author Francis Ruscetti of the Laboratory of Experimental Immunology at the National Cancer Institute: *"These compelling data allow the development of a hypothesis concerning a cause of this complex and misunderstood disease, since retroviruses are a known cause of neurodegenerative diseases and cancer in man".* The AFP report continued: *"Retroviruses like XMRV have also been shown to activate a number of other latent viruses. This could explain why so many different viruses…have been associated with CFS".*

The NIH National Cancer Institute's press release ("Consortium of Researchers Discover Retroviral Link to Chronic Fatigue Syndrome") said: "*Scientists have discovered a potential retrovirus link to chronic fatigue syndrome….****'We now have evidence that a retrovirus named XMRV is frequently present in the blood of patients with CFS. This discovery could be a major step in the discovery of vital treatment options for millions of patients'*** *said Judy Mikovits, leader of the team that discovered this association….The virus, XMRV, was first identified by Robert H Silverman, professor in the Department of Cancer Biology at the Cleveland Lerner Research Institute…****The research team not only found that blood cells contained XMRV but also expressed XMRV proteins at high levels and produced infectious viral particles****…These results were also supported by the observation of retrovirus particles in patient samples when examined using transmission electron microscopy. The data demonstrate the first direct isolation of infectious XMRV from humans….****Retroviruses like XMRV have also been shown to activate a number of other latent viruses. This could explain why so many different viruses…have been associated with CFS****. Dan Peterson, medical director of WPI, added:* ***'Patients with CFS deal with a myriad of health issues as their quality of life declines. I'm excited about the possibility of providing patients who are positive for XMRV (with) a definite diagnosis and, hopefully very soon, a range of effective treatment options'*** *"* (http://www.cancer.gov/newscenter/).

Science News pointed out: ***"The researchers also show that the retrovirus can infect human immune cells…'This is a very striking association – two thirds of the patients'*** *says John Coffin, a virologist at Tufts University in Boston….****Mikovits asserts that the retroviral infection might result in an immune deficiency that leads to chronic fatigue symptoms. Retroviruses are known to attack the immune system, with HIV***

being the best-known example. In this study, researchers showed that XMRV infected immune cells in the blood…Retroviruses can awaken latent viruses already in cells. It is possible that symptoms are caused not by XMRV but by other viruses that it activates".

The Scientific American noted: ***"Chronic fatigue…is a misnomer. The syndrome often has more to do with immune system abnormalities than pervasive tiredness****…XMRV has recently been linked to strong cases of prostate cancer. Like CFS, this cancer involves changes in an antiviral enzyme (RNase L)…To find the virus, Mikovits and her team studied documented cases, such as CFS outbreaks in a symphony orchestra in North Carolina and in Incline Village, Nevada. '****We found the virus in the same proportion in every outbreak'****, she says….****Experiments in Mikovits' lab proved that the retrovirus can be transmitted via blood by infecting healthy cells drawn from volunteers with material from XMRV-positive CFS patients"***.

Ewen Callaway (New Scientist) also quoted Mikovits as confirming that her team had found antibodies against XMRV in 95% of nearly 300 patients they tested, but these further results have yet to be published in a journal. Antibodies are a more sensitive test than looking for viral genes, as they pick up people who have had XMRV in the past, not just those who still have it. Callaway noted that Mikovits also pointed out a very significant fact: not only do characteristics of the virus match the symptoms of (ME)CFS, but **viruses related to XMRV can cause blood vessels around the body to leak, a common symptom of (ME)CFS**. Quoting Jonathan Kerr of St George's University of London, Callaway said: " *'XMRV infection of natural killer cells may affect their function…This does fit"*. Callaway continued: "That sentiment is echoed by John Coffin…*'This looks like a very, very interesting start', he says. 'It's not impossible that this could cause a disease with neurological and immunological consequences' "*.

The UK's Daily Telegraph proclaimed on 9th October 2009: "*Most cases of chronic fatigue syndrome or ME may be linked to a virus, according to research that could lead to the first drug treatments for the disorder that affects millions around the world…Symptoms…can be as disabling as multiple sclerosis…Dr Mikovits' team said further research must now determine whether XMRV directly causes CFS, is just a passenger virus in the suppressed immune systems of sufferers or a pathogen that acts in concert with other viruses that have been implicated in the disorder by previous research"*.

Also on 9th October 2009, The Independent's Science Editor, Steve Connor, reported the ground-breaking research on the front page. He said that Dr Judy Mikovits, senior author of the study and Director of Research at the Whittemore Peterson Institute in Reno, Nevada, had confirmed that *"further blood tests have revealed that more than 95% of the patients with the syndrome have antibodies to the virus, indicating that they have been infected with XMRV…'With these numbers, I would say yes, we have found the cause of chronic fatigue syndrome. We also have data showing that the virus attacks the human immune system' "*. **Connor reported that Dr Mikovits is testing a further 500 blood samples gathered from chronic fatigue syndrome patients diagnosed in London. *"'The same percentages are holding up' she said"*.**

Of note is that the UK's NHS Knowledge Service (for several years the NHS has persisted in includng ME/CFS in its mental health minimum dataset despite frequent requests to categorise it correctly) said: "*CFS affects a range of organs in the body, and patients show abnormal immune system function…one theory is that certain viruses trigger the disease…Overall, samples from the people with CFS were 54 times as likely to contain viral sequences as samples from healthy controls"* (http://www.nhs.uk/news/2009/10October/Pages/Does-a-virus-casue-ME.aspx).

On 8th October 2009 Hillary Johnson, outspoken author of "Osler's Webb: Inside the Labyrinth of the Chronic Fatigue Syndrome Epidemic" (Crown Publishing Inc, New York, 1996), was blunt: "*A generation of quacks and sub-par investigators will be in retreat…The real scientists have arrived and they'll be studying XMRV-associated neuro-immune disease, (i.e.) XAND….the Whittemore Peterson Institute and its collaborators have turned a 20-year crime story back into a science story.* ***Mikovits found XMRV in a sample of frozen blood that had been saved by Dan Peterson as long ago as 1984. The blood happened to have been drawn from a patient who went on to die of mantle cell lymphoma, another disease XMRV is suspected of causing…****the failure of the*

Centres for Disease Control to respond professionally and rationally when presented with a novel retrovirus in patients and their close contacts in 1991 by Elaine De Freitas needs to be revisited immediately…We've monitored the agency's wilful ignorance of – indeed, their extreme hostility to – the science in this field….if it turns out that their failure to replicate Elaine de Freitas' findings of a novel retrovirus in this disease, followed by their attempt to destroy her professional reputation, was purposeful, then…the CDC is as much a crime scene as it is a federal science agency. ***How could our government and the governments of other nations dismiss and then ignore millions who suffered from 'an infectious disease of the brain' as Hilary Koprowski of the Wistar Institute called it publicly in 1992. Koprowski was an expert in neurological diseases – he knew one when he saw one…****they will talk about the dangers of scientific bias and the near-criminal manner in which a disease could be defined, for so long and in spite of so much contrary evidence – as a personality disorder…****The years of our lives during which thousands of research papers were written by psychiatrists purporting to explain away a life-destroying disease with discussions of personality disorders, exercise and activity phobia, malingering, hysteria, sexual abuse, school phobia, attention-seeking behaviour must be respected (and) the papers saved for posterity. Princeton English professor Elaine Showalter's book equating this disease with fantasies of alien abduction probably deserves its own shelf in this pantheon of the grotesque…All these works will be examined, in time, by researchers who seek to understand the human capacity for delusion, ignorance and greed"* (http://www.oslersweb.com/blog.htm?post=638469).

Particularly notable was the BBC's reporting of the comments of Tony Britton, the (lay) Publicity Manager at the UK ME Association: *"This is fascinating work, but it doesn't conclusively prove a link between the XMRV virus and chronic fatigue syndrome or ME"*, a statement that should be compared with what was published in Science: "*we have discovered a highly significant association between the XMRV retrovirus and CFS"* and with the WPI press release: "*This finding clearly points to the retrovirus as a significant contributing factor in this illness".*

It is regrettable that the UK ME Association's Publicity Manager seems not to distinguish between proving a conclusive cause and proving a direct link, a link that certainly satisfied the many prestigious referees who advised the journal Science.

It also satisfied Richard T Ellison III, Professor of Medicine, Molecular Genetics and Microbiology in the Division of Infectious Diseases and Immunology at the University of Massachusetts Medical School (Deputy Editor of Journal Watch Infectious Diseases since 1988), who commented: ***"These studies provide clear evidence that active XMRV infection occurs in many CFS patients"*** (Co-Cure RES: 22nd October 2009).

Moreover, as Hillary Johnson reported in the New York Times on 21st October 2009, Judy Mikovits had worked for the National Cancer Institute for 22 years and she was impressed that Dan Peterson *"had built an extraordinary repository of more than 8,000 chronic fatigue syndrome tissue samples going back as far as 1984…****What (Mikovits) found was live, or replicating, XMRV in both frozen and fresh blood and plasma, as well as saliva. She has found the virus in samples going back to 1984 and in nearly all the patients who developed cancer.*** *She expects the positivity rate will be close to 100% in the disease.* ***'It's amazing to me that anyone could look at these patients and not see that this is an infectious disease that has ruined lives,' Dr Mikovits said****. She has also given the disease a properly scientific new name: X-associated neuroimmune disease (XAND)".*

On 20th October 2009 Judy Mikovits herself was interviewed; she said: ***"John Coffin is a member of the US National Academy of Sciences. No greater authority on these viruses exists. Three members of the US National Academy of Sciences reviewed this work and all are convinced of the science…they are convinced of the infection and the public health risk"*** (http://merutt.wordpress.com/tag/chronic-fatigue-syndrome/).

Interviewed live by Rene Montagne, when asked why people thought sufferers don't really have a disease, Dr Daniel Peterson, medical director of the WPI, was clear: "*I think the reason for that is the abnormalities of the immune system are initially very subtle. And if a physician does just routine testing – you find they're normal. It isn't until you look at the immune system that you realise there's substantial dysregulation…It's very similar to asymptomatic carriers of HIV. They look just fine until time passes and their illness evolves and more symptoms are found.* ***But I never felt this was predominantly a psychiatric disease or malingering. There was never any***

evidence to support that theory…*Once it was demonstrated that the patients had impairment of the natural killer cells function, regardless of what country they were in, we knew that there was immune impairment…Back in the 1990s, I was associated with Temple University and researchers (who) looked at the antiviral pathway…found very substantial abnormalities in the patients who had chronic fatigue syndrome. And the illness is totally compatible with a viral illness that just doesn't go away"* (http://www.npr.org/templates/story/story.php?storyId=113650222).

Following the (re)discovery of a direct link between a retrovirus and ME/CFS, there has been much internet traffic about the dismissing and ignoring by US agencies of state of Dr De Freitas et al's work two decades ago that demonstrated a potential retroviral link, particularly in relation to possible transmission via blood products.

This down-playing has been ascribed by some people to (i) a possible UK/US collaboration over the use of biowarfare agents, including borrelia ("US Government Admits Lyme Disease Is A Bioweapon": Co-Cure ACT: 1st January 2006: http://www.indymedia.org.uk/en/2005/11/328067.html and http://www.lyme-rage.info/elena/statejun06.html); (ii) the CDC's apparent determination to prevent at any cost public panic over the emergence of another AIDS-like pandemic and (iii) the wish to protect insurers from having to make payments for another chronic disease, factors that may be instrumental in Dr Bill Reeves' dismissive comments about the latest discovery of an association between a retrovirus and ME/CFS:

- the journal Nature reported: "*William Reeves, principal investigator for the Centres for Disease Control and Prevention (CDC)'s CFS public health research programme, says the findings are* ***'unexpected and surprising'*** *and that it is* ***'almost unheard of to find an association of this magnitude between an infectious agent and a well-defined chronic disease, much less an illness like CFS…Until the work is independently verified the report represents a single pilot study'.*** *He also notes that CFS…likely arises from a combination of many factors"*

- the Los Angeles Times also reported Reeves comments, adding his comment that: ***"****It is extremely difficult to prove causation with a ubiquitous virus like XMRV, and it* ***'is even more difficult in the case of CFS, which represents a clinically and epidemiologically complex illness'*** *he said. Unfortunately, Reeves said,* ***the major flaw of the study is that there is not enough information about how subjects were selected to rule out any bias in choosing them"***

- the New York Times (13th October 2009) reported Reeves as saying ***"he was surprised that a prestigious journal like Science had published it****….We and others are looking at our own specimens and trying to confirm it…****If we validate it, great. My expectation is that we will not****'….Many patients and a community of doctors and researchers who specialise in the syndrome take issue with the (CDC's) approach to the illness and the way it defines who is affected. They claim that the CDC includes people whose problems are purely psychiatric, muddying the water and confounding efforts to find a physical cause"* (it is the case that the CDC now uses Reeves' own (2005) definition that does not distinguish between CFS and major depressive disorder, so it is to be anticipated that the CDC will not replicate the Mikovits et al findings).

Against this background, there are mounting calls for the removal of Dr Reeves from his position as principal investigator of the CDC's CFS research programme ("Support the 500 Professionals of the IACFS/ME – Reeves Must Go"):

"*On May 27th and May 28th, 2009, the Chronic Fatigue Syndrome Advisory Committee (CFSAC) convened in Washington, D.C. Among their recommendations to the Secretary of Health and Human Services was a call for new and progressive leadership at the CDC's ME/CFS research division. Under Bill Reeves' regime, funding has routinely decreased and increasingly broad definitions which have ceased to have any clinical meaning or research value have been implemented…. Under Reeves' direction the CFS program is being slowly strangled….* ***What does Reeves say about Mikovits' recent discovery? Without doing any study or due diligence, Reeves dismisses the***

findings*… Inaccurate stereotypes persist because Bill Reeves has not been accurately educating the public on the seriousness of this disease"* (Co-Cure ACT: 25th October 2009).

Comments such as that by Tom Kindlon from the Irish ME/CFS Association reflect the position of many in the international ME/CFS community: "***What does he mean 'much less an illness like CFS'****? CFS is much more like a chronic viral disease than most chronic diseases.* ***Why is he heading a programme based in the viral section of the CDC if he has this attitude?****"* (Co-Cure ACT:8th October 2009).

In her customary robust manner, Hillary Johnson in the US is scathing about Bill Reeves: ***"There isn't anything Reeves said to the press that was scientifically correct, one of the scientists associated with this work told me recently…How about Bill's comment, expressed to the New York Times, that he was 'surprised' a 'prestigious journal like Science' had published the study…Frank Ruscetti isolated the first human retrovirus infection HTLV (Human T-cell Leukaemia / Lymphoma Virus) at the National Cancer Institute 30 years ago. Bill thinks Ruscetti doesn't know what he's doing? Bob Silverman was a co-discoverer of XMRV; Silverman doesn't know what he's doing? Science was duped?*** *Is he kidding? Bill also suggested the paper didn't mean much because he, Bill, didn't know how the patients were selected. The patients were clinically defined by every medical criteria, including the CDC's. What more does Bill want? By now, most will have heard about Bill's comment that XMRV is a ubiquitous virus. That must have been a whoo-hoo moment for the Science collaborators. These collaborators didn't just arrive on the scene last month…they knew going into this work what the CDC did to Elaine De Freitas and her retrovirus finding in 1991. They understood the politics. They were aware of the agency's multi-million dollar propaganda war on a million very sick people. They were prepared. They CDC-proofed this study. The rigour in the Mikovits-Ruscetti-Silverman paper was such that Science had to take the paper"* (Co-Cure NOT: 25th October 2009).

Notably, Dr Stuart Le Grice, head of the Centre of Excellence in HIV/AIDS and cancer virology at the National Cancer Institute went on record saying: *"NCI is responding like it did in the early days of HIV"* (in other words, by dismissal and denial of the significance). As Cort Johnson observed: *"Neither the CDC nor the NIH (with the exception of NK cells) have shown any interest in pathogens of the immune system in over ten years. Research into ME/CFS has declined precipitously in both institutions over the past five years"* (http://aboutmecfs.org/blog/?p=920).

In response to an article in Nature by Lizzie Buchen who quoted Judy Mikovits as saying: "*I can't wait to be able to tell my patients…It's going to knock their socks off. They've had such a stigma. People have just assumed they were just complainers who didn't handle stress well"*, a comment posted on Nature News by John Smith captures the reality: "*The nature of this seriously disabling disease has taken so long to establish because of the paucity of serious biomedical research into the condition and the failure of government to support such research.* ***As a scientist who has suffered from it for over 25 years following viral infection I have watched, appalled, as scientific politics have deflected funding away from biomedical studies towards psychosocial ones. This is nothing short of a scientific scandal"*** (http://www.nature.com/news/2009/091008/full/news.2009.983.html).

In the UK, Simon Wessely is similarly unpopular, and for similarly well-founded reasons.

On 5th February 1999 that the New Statesman carried an article by Ziauddin Sardar about Wessely (titled "Ill-defined notions") in which Sardar wrote:

"Once upon a time, if you were sick, you were really sick. You had a collection of recognisable symptoms. Now if you are ill there may not be a 'cause'. You may be suffering from something but you may not be ill at all — according to the medical establishment anyway (because) the 'cause' of some illnesses is better seen as a lifestyle than a pathogen.

"Sickness is no longer simply a personal matter; it has become social, political, beaurocratic….When is someone sick, really sick? Who decides? By what criteria and procedures?…The only thing that is certain is that the patient himself / herself has little power and cannot answer any of these questions. You are ill only when someone says you are ill.

"Consider syndromes. Once this was a name for a collection of symptoms for which no clear cause had yet been found. Now it stands for a bunch or bunches of symptoms lacking even the security of certainty that they are actually there…Most notorious is "chronic fatigue syndrome". At the far extreme, it is known as "ME"…From its first recognition as a large-scale problem... .horror stories abound of people (some of them children) whom the medical and psychiatric experts considered to be just faking...

"The same can be said of Gulf War syndrome….again, there are lots of nasty symptoms: mild to moderate chronic fatigue, double vision, severe urinary and sexual problems, memory loss, joint and muscular pain — to start with…But even though 400 veterans have actually died and some 5,000 are suffering from illnesses related to Gulf War syndrome, the syndrome does not officially exist.

"All the actors involved in this drama have their own perspective... .the government with avoiding paying compensation at all costs. So one would expect the Ministry of Defence to deny the existence of Gulf Way syndrome and it does, operating on the simple basis of "no bug, no dosh".

"...this makes life very hard for sufferers. They not only have to survive their disease: they must also fight for elementary decency. And that is a long and bitter task in itself.

"But what of researchers? Why should they deny the existence of Gulf War syndrome? The struggle over recognition hinges on research. But this research is a totally different exercise...How do you investigate this mess of symptoms? Not with biochemistry, but with psychiatry.

"The new societal syndrome of syndromatic diseases requires a new speciality, a syndromologist. Fortunately, one is to hand. His name is Professor Simon Wessely, consultant psychiatrist at the School of Medicine, King's College, London.

"Wessely has been arguing that ME is a largely self-induced ailment that can be cured by the exercise programme on offer at his clinic.

"Recently he published the results of "the most definitive study" of Gulf War syndrome in.. .the Lancet... .It concluded — surprise, surprise — that there is no such thing as Gulf Way syndrome.

"So Wessely, who occupies a key position in our socio-medical order, denies the existence of Gulf War syndrome, just as he denies the existence of ME.

"Clearly, he is a follower of Groucho Marx: 'Whatever it is, I deny it'. Not surprisingly, lots of people hate him.

"If Simon Wessely is our syndromologist-in-chief, who has chosen and vetted him for that post, and by what criteria and procedures? Where is the debate over the shaping of such research?…When will we have the first officially sponsored study of such a problem which the sufferers do not have the occasion to call a whitewash?".

Since at least 1994, when the CFIDS Chronicle published an article titled "The views of Dr Simon Wessely on ME: Scientific Misconduct in the Selection and Presentation of Available Evidence" (Spring 1994:14-18), valid criticisms of Wessely have continued to mount, some of which can be accessed at http://www.meactionuk.org.uk .

In his article in New Scientist on 9th October 2009 (referred to above), Ewen Callaway noted Professor Wessely's position regarding the discovery of XMRV in CFS patients: "*Wessely points out that XMRV fails to account for the wide variety of other factors associated with the CFS, including childhood trauma…'Any model that is going to be satisfactory has to explain everything, not just little bits' he says".*

Wessely's belief that childhood trauma causes ME/CFS takes no account of those who had a happy, secure childhood within a stable and loving family but who still developed severe ME/CFS.

Similar points are reflected in the many online comments posted to the New Scientist. These were highly critical of Wessely's dismissive attitude, and provided examples of the adverse impact on patients of his ill-grounded beliefs about ME/CFS, for example:

"Dr Wessely had the chance to prove he had some kind of humility with regard to his disgraceful behaviour towards 'CFS' "

"Now if that's not the sound of a desperate drowning man clinging to the sinking wreckage of his fatally flawed theory for ME. Give it up, Wessely, sink to the bottom of the sea, vanish without trace. The time has come once and for all to banish these primitive psychological theories to the dustbin of medical history, where they so rightfully belong"

"Completely agreed – Simon Wessely, the medical establishment and local authorities that have taken children into care, sectioned adults, forced harmful treatment, ruined lives, should be made to apologise to every single one of their victims, not only here but worldwide"

"Holding a different evidence-based view-point is one thing – ignoring evidence and letting ego condemn patients to grotesque suffering and death as a physician is evil and should be dealt with as such"

"I look forward to seeing the psychological research by Professor Wessely published in the journal Science"

"I was diagnosed with ME in 1992 –3.. …I'm a former clinical specialist in life-support technology, qualified in medicine, perfusion science and life-support technology, so I know a bit about all this. I empathise with anyone who has genuinely suffered this condition, especially when they have not had good treatment from their own doctors"

"To the Editor: It remains a mystery as to why you bother including the unsubstantiated opinion provided by Dr Simon Wessely. He continues to profit from the prescription of cognitive therapy for this serious illness, despite the fact that the majority of patients fail to benefit from such interventions. By any other model, insistence upon cognitive therapy as the default model for treatment should constitute malpractice"

"I saw on my doctor's notes that the symptoms were all in my 'mind'. This was despite a low white cell count, inflamed spleen and swollen lymph nodes. Yep, the low white cell count was because of my 'mind'. If they dismissed cancer this way the overpaid morons would be sued for malpractice;

"Those physicians may have some red-faced explaining to do if this research pans out"

" 'Red-faced' – no, they should be sued for negligence. Sorry, but I was damn near killed by such idiocy so I have not the slightest sympathy for such bigoted physicians…I want several prominent persons responsible for this terrible abuse of millions of ill people across the globe criminally charged and tried for negligence…Many people have DIED because of this, either by direct abuse by doctors, or by disdainful refusal to aid, or actively preventing research into physical causes. Sophia Mirza is only one such victim, most others just sank without trace as it was 'inconvenient' and their death or suicides were 'all their own fault as it was all in their heads'. But when a physician deliberately ignores his duties because of prejudice – that, sir, is ABUSE. Imagine how an MS sufferer would feel if they were ignored, abused, even sectioned by the very physician who swore an oath to help them. And then the very person at the top of the pyramid of abuse was allowed to publish articles about MS…"

"But, Simon, you said they thought themselves sick…Wessely points out that XMRV fails to account for the wide variety of other factors associated with the CFS, including childhood trauma….but Professor Wessely was quite happy to lead nations to think that these unfortunate people were all suffering from 'abnormal illness beliefs'. Why was he so happy to ignore biomedical research which demonstrated that this disease was not a mental illness?"

"Simon Wessely…(has) a lot to answer for…I have yet to meet someone with ME who hasn't inspired me with their strength. It's just a shame there is so much to fight against"

"The idea that ME was somehow linked to childhood trauma was always nonsense…Way back when I was first ill, researchers were looking for a retrovirus. The problem was that no-one would fund them and allow then to continue their work. They were repeatedly turned down and their work blocked. This retrovirus should have been discovered at the same time as AIDS and the last few miserable decades of my life could have been avoided…No more excuses and no more psychobabble"

"Tragically for sufferers, the psychological zealots are ruling the asylum and they have steered successive definitions away from viral, inflammatory disease and to their beloved 'unexplained fatigue' and disingenuous 'psychological factors'. Mediocre findings of CBT/GET have been spun more than a New Labour carousel leading a character assassination on the ME community, creating an ideological distortion of the very presentation of the disease, whereby misled doctors dismiss such unfortunate patients as 'pond life' or 'ME lunatics' and deny even the most severely affected (eg bedbound) patients access to investigation, treatments, monitoring, advocacy and education of social and welfare support networks, while taking no interest in/dismissing the literature themselves. Cue great neglect, suffering, exploitation, wasted generations and premature deaths. Will the psych/med profession apologise? Just as with past outrages against multiple sclerosis (and) Parkinsons, will they hell" (http://www.newscientist.com/commenting/browse;jsessionid=5E5EAC8B3582B288ADB3A7F9F2D0611A?id=dn17947).

Other similar comments about Wessely were posted in response to The Independent's coverage of the XMRV discovery, for example:

*"**This is the time for Simon Wessely to walk away and shut the door. We don't want to see him ever again mentioned in relation to this disease. Didn't he read the news – 500 blood samples from London are being tested and the figures are holding up**…I have spent my entire adult life with this disease and I would like to have some illness-free years before I die. **The UK government and medical research council squandered millions chasing a psychological cause"***

"I know as bad as things are in the U.S. in regard to ME, the UK seems even worse. That Wessely guy is a total moron. This disease has so many consistent biological abnormalities across the ME/CFS population and they are continually being ignored. Will these people ever listen?"

***"Wessely, it is time for you to accept the truth and give up**. I have had ME for 7 years and it has completely consumed my life. **Money put into the research has been very limited, mostly due to the political connections of Wessely, his partner and the labour party. I know. I worked in there**"* (Wessely's wife, Dr Clare Gerada, was / is a senior policy advisor to the Department of Health; she is Vice Chair of Council of The Royal College of General Practitioners and is Chair of the RCGP Medical Ethics Committee)

"It's in Simon's mind: I have lost 15 years to CFS and exhortations that CBT and graded exercise (which I have done in spades) have on more than one occasion pushed me to the edge…What a pathetic scam to let millions suffer on a pretence"

*"I wholeheartedly agree with comments made against Simon Wessely. His title says it all – professor of psychological medicine. **Unfortunately there are a great many people like him who have held back the frontiers of modern research by dismissing the findings and instead promoting psychological causes"***

"Mr Wessely's views. Time to put your cards on the table. I find it interesting that Wessely is so keen to keep ME 'all in the mind', especially with a growing mass of evidence to suggest otherwise. I'd like to see his funding resources revealed…I'm sure that behind closed doors there is more going on to douse the flame of truth than we actually know about".

"I was very saddened to read Simon Wessely's comments…and personally feel that the psychological explanation for ME/CFS is far from satisfactory"

"I worked in the Civil Service for both Jacqui Smith and Alan Johnson (the latter is currently Secretary of State for Health). *Once I became disabled with CFS I was horribly bullied by the Civil Service. It was a truly terrible time, trying to cope with a life-altering disability and an employer who did not care"*

On other sites (for example; http://www.meactionuk.org.uk/wessely.html), people recalled what Wessely has said and published about ME/CFS in the past, for example:

"What lies behind all this talk of viruses and immunity?…..Talk of viruses and the immune system is now embedded in popular consciousness….Viruses are an attribution free from blame…there's no blame, no shame and no stigma*….****And*** (mocking) ***here is the virus research doctor himself to protect us from that shame….And what is it he delivers? Respect"*** (Microbes, Mental Illness, the Media and ME: The Construction of Disease. 9th Eliot Slater Memorial Lecture, Institute of Psychiatry, 12th May 1994).

"***Wessely sees viral attribution as somatisation par excellence"*** (Helen Cope, Anthony David, Anthony Mann. Journal of Psychosomatic Research 1994:38:2:89-98).

In a reply to someone who wrote to him on 12th November 2009 asking for his response to the XMRV findings, Wessely replied: *"Could be a real breakthrough, even if I still don't understand how they made the leap from prostate cancer to CFS"*, which seems to indicate that Wessely remains ignorant of or else does not understand what Judy Mikovits et al said: *"**both are linked to alterations in the antiviral enzyme RNase L**"*, a link that was clearly explained by David Bell in his Lyndonville News, volume 6, number 2, October 2009: *"**XMRV was first linked to human disease by Robert H Silverman, PhD at the Cleveland Clinic in patients with prostate cancer who also had a defect in the RNAse L antiviral pathway. As this pathway has been known to be abnormal in CFS, it was reasonable to search for the virus in CFS**"*. Wessely then seemed to deny the association with XMRV and cancer: *"I am worried that 20% of the CFS patients seem to have lymphoma (ie cancer), which might be fascinating for our knowledge of cancer **but really isn't relevant for CFS**"*. Apparently adopting the same stance as Bill Reeves in the US, Wessely continued: *"I would be very surprised indeed if others find rates of XMRV at the same level as this paper"* (Co-Cure ACT: 12th November 2009).

There is international recognition that Wessely *"is employed by the Ministry of Defence and NATO (he chaired a committee on psychological responses to WMD – weapons of mass destruction) and heavily backed by corporate interests to deny the reality of chronic illnesses such as ME/CFS, Gulf War Illness, Lyme Disease, Multiple Chemical Sensitivity and others…**Wessely's name is known to the thousands of sufferers of chronic illnesses in Britain and abroad who have been hurt by his philosophy…For years Wessely has been the outspoken proponent of the view that chronic physical conditions such as Gulf War Illness, ME/CFS, fibromyalgia, Lyme Disease, MCS and others are simply 'all in the head' of the sufferer. This view has received great support from the Government and from the Army, both here and in America.** It has also been enthusiastically promoted by insurance companies and the Department for Work and Pensions. **Millions of public research funds have gone into the pockets of psychiatrists following the Wessely school of thought. The result: seriously ill patients have been denied recognition and treatment, disability benefits and dignity. They have been ridiculed by doctors and vilified in the press. Stigmatised by Wessely and his followers as malingerers, hypochondriacs, or simply 'mad', sufferers of chronic physical illnesses have been left untreated for years, sometimes ending up paralysed, amnesic or even dying**. Some commit suicide under the pressure of isolation and never-ending pain. **Providing no evidence base for his conclusions, Wessely nevertheless rides roughshod over published medical studies linking vaccine damage, chemical exposure etc with Gulf War Illness (and) toxic chemical exposure (and) viruses with fatiguing illnesses. He does not disprove the evidence of physical causes for these diseases – he just ignores it**"* (http://tinyurl.com/ybqcvs9).

As long ago as 1998, in his article "Dr Simon Wessely: Prophet or Profit?", Dr Ken Jolly, a GP in New Zealand who had to give up his medical practice because of ME/CFS, published his concern that Wessely et al had come to dominate thinking about ME/CFS even in New Zealand, saying that they had achieved such influence by producing vast volumes of papers on CFS and obtaining funding for their own work. Jolly was forthright:

"I feel it is time sufferers in NZ became aware of his growing influence. The existence of this influence is no new to UK sufferers and it has affected how they are being treated, as well as their accessibility to aid and financial assistance. Clinicians with opposing views are being sidelined by most of the prestigious medical journals. Why this is so is unclear. Simon Wessely is very politically astute (and) has been able to sway many to his way of thinking. He has also developed a 'patter' which he uses to convince patients of the rightness of his model. In reality, this is a smokescreen which effectively covers his true underlying beliefs. ***But 'the clincher' for convincing many medcial scientists of any theory is to back it up with reliable research data. He and his colleagues have 'appeared' to do this, almost putting an end to the oppositional cries from the physical camp. However, these trials have been flawed in every way imaginable…Unfortunately people like Simon Wessely, in my opinion are not only using up large amounts of valuable research monies but are also diverting research along blind paths…*** *I will now attempt to summarise Simon Wessely's and colleagues' views about ME. The reason I have chosen to mainly discuss Simon Wessely rather than the others of the group is because it so often appears that he is the mouthpiece for their statements".*

Dr Jolly then lists some of the more notorious of Wessely's published views, including Wessely's belief that CFS is merely the extreme end of normal fatigue which, as Jolly points out, totally ignores the cyclic nature of the disorder that is a pattern commonly seen in autoimmune diseases. Jolly also points out that Wessely's claim that ME/CFS patients' symptoms are caused by hypervigilance towards normal bodily sensations does not explain why the same symptoms are reported by thousands of patients worldwide (who may not even speak the same language). Jolly notes that many physically-based research findings *"have frequently been ignored for the (Wessely) model to continue to fit".* Jolly is particularly scathing about Wessely's view that patients perpetuate their own illness: "*This is insulting to their intelligence. In my experience patients undergo enormous financial, social and relationship losses because of this illness. Additionally, they are prepared to go to almost any lengths to get better – NOT the actions of people perpetuating a condition associated with non-activity"* (http://tinyurl.com/ybqcvs9).

As Dr Jolly further noted: "*The effect that Simon Wessely may have in the future on how doctors view ME cannot be underestimated. His viewpoint seems to have pervaded the thinking of the medical establishment in the UK. The most worrying aspect is that these theories suit those who are politically in charge and many institutions and governments are already being seduced to this way of thinking…Why Simon Wessely has pursued this theory with such tenacity somewhat eludes me.* ***He has encountered massive opposition from many quarters****".*

An internet search will quickly reveal that there is extensive outrage about Simon Wessely and his colleagues' unproven beliefs, not only from ME/CFS patients and their long-suffering families, but also from international medical scientists and clinicians who are not blinded by ideology or vested interests.

In his article in The Independent on 9th October 2009 (referred to above), Steve Connor also quoted Professor Simon Wessely's views on the implications of the XMRV discovery: *"Other researchers emphasised that the numbers published so far are too small to conclude anything about the cause of chronic fatigue syndrome. 'It's spectacular but needs replicating. And I hope that no-one is thinking of prescribing anti-retrovirals on the basis of this, said Simon Wessely, professor of psychological medicine at King's College, London****. 'It's very preliminary and there is no evidence to say this is relevant to the vast majority of people in the UK with the condition'*** *".*

However, in a Leading Article that same day, The Independent said:

"…for many years doctors argued that Chronic Fatigue Syndrome didn't exist. They refused even to dignify it with the name Myalgic Encephalomyelitis. ME, they said, was just 'me' writ large… Scientists could be on the brink of a breakthrough. We must hope they are. That would – at least – go some way to compensating for the shameful manner in which sufferers were treated for so long by the medical profession".

On 29th October 2009 Professor Coffin told a Department of Health and Human Services Committee that this discovery was of ***"potentially extraordinary importance****",* not least, as Jack Johnson reported (Co-Cure NOT:16th November 2009), because it means validation and hope for millions of people suffering from

(ME)CFS, often thought by many to be nothing more than the product of neurosis and even laziness and, as Jack Johnson pointed out: "***CFS has long been thought to be linked to retroviral infection***".

As noted in "Denigration by Design? A Review, with References, of the Role of Dr (now Professor) Simon Wessely in the Perception of Myalgic Encephalomyelitis (Up-date) Volume II (http://www.25megroup.org/denigration%20by%20design/denigration%20contents.htm), it seems that to Wessely and his closest associates, the belief of the moment represents the only truth.

They would do well to remember that in the early 1600s, King James I of England (who was also King James VI of Scotland) wrote a book called "Demonology" and that book helped to send to their death women known as the Lancashire witches. Countless innocent women were persecuted, tortured and executed as witches, having been forced into admitting things they did not do, the majority being people who suffered from mental illness.

Incredibly, it was not until the 1950s that the Witchcraft Act was repealed in the UK. This must surely serve as a salutary reminder that the belief of the time (currently, that ME/CFS is a behavioural disorder) is not necessarily the truth, even though it might be promoted as the truth.

It is fair to say that the views of Wessely and his close colleagues (including those involved with the PACE Trial) are held in contempt by many people – medical and lay alike – who have to deal with the reality and severity of ME/CFS, yet injustice for those with ME/CFS continues. Cases of untold suffering and despair continue to accumulate, and this is very significantly because of the influence of the Wessely School.

One can but pray that along with his colleagues Peter White, Michael Sharpe and Trudie Chalder, Wessely's power and influence – unlike that of demonology – will not remain enshrined for the next 350 years and that medical science may at last have provided the means to right the wrongs that the Wessely School have done so much to perpetrate upon those with ME/CFS.

That such wrongs exist in the US is further demonstrated by the testimony of Kenneth Friedman on 30th October 2009 before the CFS Advisory Committee (Co-Cure NOT:MED: 4th November 2009). Friedman, a medical school professor at the Department of Pharmacology and Physiology, New Jersey Medical School, said:

"*I have been asked to comment upon the status of Chronic Fatigue Syndrome education in the United States.*

"The Director of the Office of Ethics and Compliance has informed me that my off-campus activities relating to CFS which include testifying before this Committee, serving on this Committee, providing continuing medical education courses, establishing medical student scholarships and assisting with healthcare legislation are not part of my responsibilities as a University Professor.

" I am told that I will be punished with a penalty as severe as termination of my employment for these activities.

"I am not a unique target. Colleague Ben Natelson (an ME/CFS researcher who was Professor in the Department of Neurosciences at New Jersey Medical School) *has left the same school.*

"A different medical school has refused to permit access to their medical students to discuss CFS.

"A statewide healthcare provider…refuses to permit a CFS training session for their physicians.

"The failure of the CDC to convince the medical-academic establishment of the legitimacy of CFS, and the urgent need for its treatment, has created this environment".

Could it be said that the Wessely School has created a similar environment in the UK and that the MRC PACE Trial is part of that constructed environment, just as the NICE Clinical Guideline and the actions of NICE which resulted in the failure of the Judicial Review were also part of it?

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