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CORONAVIRUS AND CFIDS/ME – ARE PATIENTS AT GREATER RISK?

By Alan Cocchetto, NCF Medical Director – Copyright 2020

The COVID-19 pandemic, also known as the coronavirus pandemic, is an ongoing pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV2). The outbreak was first identified in Wuhan, China, in December 2019. The World Health Organization declared the outbreak a public health emergency of international concern on January 30 and a pandemic on March 11. As of May 27, more than 5.61 million cases of COVID-19 have been reported in more than 188 countries and territories, resulting in more than 350,000 deaths. More than 2.3 million people have recovered from the virus. The virus is primarily spread between people during close contact, most often via small droplets produced by coughing, sneezing, and talking. The droplets usually fall to the ground or onto surfaces rather than traveling through air over long distances. Less commonly, people may become infected by touching a contaminated surface and then touching their face. It is most contagious during the first three days after the onset of symptoms, although spread is possible before symptoms appear, and from people who do not show symptoms. Common symptoms include fever, cough, fatigue, shortness of breath, and loss of sense of smell. Complications may include pneumonia and acute respiratory distress syndrome. The time from exposure to onset of symptoms is typically around five days but may range from two to fourteen days. There is no known vaccine or specific antiviral treatment. Primary treatment is symptomatic and supportive therapy. Recommended preventive measures include hand

National CFIDS Foundation "Forum Newsletter" to be Placed Online

The NCF will now place its Forum newsletter on the homepage of its website so that all CFIDS/ME patients will have free access to its ongoing research information as well as to patient articles. The presence of the Coronavirus pandemic has compelled the NCF to examine its newsletter distribution methods. As such, the NCF has decided to move from an all paper distribution to an all-digital format to be distributed via the internet. We encourage patients to look for the next Forum newsletter on its website at www.ncf-net.com

washing, covering one's mouth when coughing, maintaining distance from other people, wearing a face mask in public settings, and monitoring and self-isolation for people who suspect they are infected. Authorities worldwide have responded by implementing travel restrictions, lockdowns, workplace hazard controls, and facility closures. Many places have also worked to increase testing capacity and trace contacts of infected persons.

Now come the real questions: Are CFIDS/ME patients at greater risk for COVID-19 infection? Likewise, could an infection with COVID-19 result in severe illness complications for patients? Although we don't have hard-lined tangible data at this time, it is easy for us to speculate how serious an infection this would be for our patients. Let's first begin with what we know. One of the highlights of CFIDS/ME is immune dysfunction. No one can argue that point. Immune dysfunction would certainly place patients in the "at risk" group for COVID19 infection. You may ask yourself, what evidence does the NCF have to suggest that this is in-fact the case? The NCF's research confirmed a key finding first identified by Dr. Kenny DeMeirleir. Most notably, the NCF was able to demonstrate that Stat1, a critically important immunological protein, was found to be grossly deficient in one-third of our NCF patient samples.

"The crisis we are facing should not make us forget the many crises that bring suffering to so many people."

Pope Francis, 2020 April Mass where he spoke of spreading a "contagion of hope".

As you may recall, this research was completed via a grant to Dr. Konstance Knox and Dr. Donald Carrigan and the results were reported at a CFIDS/ME conference. The NCF then went even further to examine fifty CFIDS/ME patient blood samples, from the NIH, with the kind assistance from the late Dr. Robert Suhadolnik. Suhadolnik discovered that all of the NIH patient samples were found to have a Stat1 deficiency. Thus, three research groups have acknowledged that Stat1 protein deficiencies exist in CFIDS/ME patients. This knowledge is critically important due to the fact that Stat1 deficiency results in compromised innate immunity to viral infections that can lead to lethal viral disease. The lack of Stat1 is the equivalent of sending a kindergartener into war. The children may try to fight but the outcome isn't going to be pretty. However, something

crucial is known about coronavirus infection that hasn't been mentioned by medical professionals. Research now shows that Stat1 deficient animals are more susceptible to infections with severe acute respiratory syndrome coronavirus (SARS-CoV). In Stat1 deficient animals, the virus was not contained in the lung but rather spread systemically and thus adversely affected the disease severity. Thus, if the animal models are correct for coronavirus infection, the NCF would expect that COVID-19 infection could prove to be especially problematic for CFIDS/ME patients given the details provided above. Please take this pandemic seriously, take appropriate precautions and most of all, be safe!

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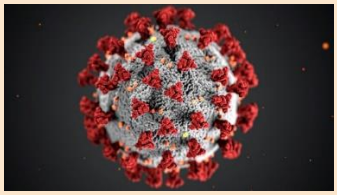
PRESIDENT'S MESSAGE

By Gail Kansky



We are living in age of a pandemic caused by COVID-19 and to help reduce the spread of the virus, we're told to remain in our own homes. In the past, other epidemics such as West Nile Virus and SARS have resulted an uptick of CFIDS/ME illnesses. Will it happen again? Will many who have gotten sick from the virus that our country is experiencing right now eventually develop our illness? The research center at Columbia University led by Dr. W. Ian Lipkin had Dr. Anthony Komaroff answer that an uptick of CFIDS/ME illnesses would be entirely possible based on past evidence. Tony is a Professor of Medicine at Harvard Medical School and the editor in chief of the Harvard Health Letter.

Dr. Komaroff said, "Sometimes, people who develop ME/CFS - after what appears to be an infection - seem to have been part of a larger epidemic." In the past, he added that many reported epidemics of CFIDS/ME around the world that have taken place in the past seventy years were studied to establish the cause but he reported that none were able to "find a cause of the initial infection". I, personally, find that hard to believe. A more believable answer would be that no country wants to admit the causative factor. Even though the scientists from Chernobyl had the cause of radiation bringing on ME/CFIDS written about in a medical journal, every country still feigns ignorance rather than admit the truth. Decades ago, we even had our entire cohort tested for radiation and all were found positive. In fact, the higher a patient tested, the more severe was their case of ME/CFIDS was.

For that matter, as this ongoing pandemic is still among us, I've felt our own government also knows and hides the treatment and the cure of CFIDS/ME. That is why, I feel, important people have been given that knowledge and moved their residence far away to help keep that knowledge to themselves. Years ago, I often had long and interesting talks with one woman who worked at the NIH who was part of the team working on CFIDS/ME. She would meet with other patients for government meetings and then, unfortunately, became sick herself. She could not keep up with her own errands as we all know how much CFIDS/ME robs you of life. Yet, a few weeks later, she was back at work. When I tried to reach her, however, I never could. Indeed, the same thing was true of others who were aware of the truth. People who were in close touch with those same people who had gotten well had the same experience. Even their private telephone numbers were no longer active.

The ongoing pandemic has also slowed the research we funded to find a treatment as the researchers are no longer allowed to continue their "nonessential" work until this world-effected pandemic is over. When the world returns to normal, I will be cheering even though, as another victim of CFIDS/ME, I will remain "sequestered" at home. An actual treatment will be coming someday even though the current pandemic will prolong the timing.

JUST ASK!

By Alan Cocchetto, NCF Medical Director – Copyright 2020

The "Just Ask" column is intended to act as a means for patients to inquire about issues related to the NCF's research activities. This column is NOT intended to act as medical advice in any way, shape or form. The National CFIDS Foundation assumes no responsibility for any action or treatment undertaken by readers. For medical advice, please consult your own personal healthcare providers.

Q: Many of my cronies, who also happen to have CFIDS/ME, get into serious discussions with me about the viral theory of this disease and poo-poo the thoughts that I have about the possibility of the cause being associated with radiation exposure. What makes radiation effects different from viruses?

A: The long and short of it can best be explained as follows. Viruses are capable of infecting limited cell and tissue types. As an example, the lungs have certain types of cells that are inherent to that tissue and organ. An influenza virus is capable of infecting those cells that are associated with the lung. However, other bodily tissues are more resistant to the effects of the influenza virus. So lung susceptibility is far more pronounced for the influenza virus than for example the kidney would be. This is typically reflected in the clinical aspects of the infection.

By comparison, radiation is a different beast and you must take into account that not all radiation is created equal. Let me explain further. Radiation is unique in that it affects all cell types and all tissue types. This is not to say that some cells and tissues aren't more resilient against the

effects of radiation but radiation effects tend to be far more broadly damaging than those associated with viruses and thus to a wider audience of cells and tissues. The 'bystander effect' is a profound example of this. One-third of the cells that surround a cell that was directly 'hit' by radiation's path will suffer cell death. We tend to think of infections as a cell-by-cell event. Radiation on the other hand can 'blitz' many more cells with a single particle. This is especially true in the case of internal alpha-radiation. The high energy associated with alpha-particles is particularly damaging when ingested or via inhalation. Radiation sickness can be either acute or chronic and it has a profound impact on the body's ability to function properly. Radiation is also known to adversely affect multiple body systems...gastrointestinal, hematopoietic, etc.

Another issue that you have with radiation versus viruses is one of duration. When you have a viral infection such as influenza, the infection acts as more of a hit-and-run event. In other words, you get infected…you begin to show symptoms…the symptoms get worse...your body fights the infection…then generally you begin to improve and your symptoms dissipate over time. That's the way most infections work. Now of course please keep in mind that this is a very simple model that I am presenting to you. By comparison, internal radiation exposure is more like 'the gift that keeps on giving.' Each radiation particle has a particular energy associated with it as well as a 'half-life.'

In the case of internal uranium exposure, high energy alpha-particles are generated. Since uranium decays slowly by emitting alpha-particles, the half-life of uranium-238 is roughly 4 billion years. So as uranium slowly decays, more and more alpha-particles are generated and as a consequence, more and more cell and tissue damage occurs in an accumulated fashion. I know that it's really crazy to think about but even after you have been dead 100 years, you will still be bombarded by alpha radiation particles. Now I ask you, can a virus do that? That is why radiation exposure can be so ominous and deadly….largely due to its widespread damaging effects. Keep in mind that I haven't even discussed what happens if you get exposed to many radiation particles…..things only get worse! Again, it is important to consider not only the type of radiation particle but the number/amount of particles as well as the duration of the exposure and the particle's half-life when examining the true effects of radiation.

"The truth is rarely pure and never simple."

Mark Twain

SELECT RECENT MEDICAL SUMMARIES

(06/01/20):

* Systematic Review of the Epidemiological Burden of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Across Europe: Current Evidence and EUROMENE Research Recommendations for Epidemiology; Estevez-Lopez F et. al; J Clin Med 2020 May 21;9(5):E1557. ABSTRACT: This review aimed at determining the prevalence and incidence of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) in Europe. We conducted a primary search in Scopus, PubMed and Web of Science for publications between 1994 and 15 June 2019 (PROSPERO: CRD42017078688). Additionally, we performed a backward-(reference lists) and forward-(citations) search of the works included in this review. Grey literature was addressed by contacting all members of the European Network on ME/CFS (EUROMENE). Independent reviewers searched, screened and selected studies, extracted data and evaluated the methodological and reporting quality. For prevalence, two studies in adults and one study in adolescents were included. Prevalence ranged from 0.1% to 2.2%. Two studies also included incidence estimates. In conclusion, studies on the prevalence and incidence of ME/CFS in Europe were scarce. Our findings point to the pressing need for well-designed and statistically powered epidemiological studies. To overcome the shortcomings of the current stateof-the-art, EUROMENE recommends that future research is better conducted in the community, reviewing the clinical history of potential cases, obtaining additional objective information (when needed) and using adequate ME/CFS case definitions; namely, the Centers for Disease Control & Prevention-1994, Canadian Consensus Criteria, or Institute of Medicine criteria.

* Intravenous Cyclophosphamide in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. An Open-Label Phase II Study; Rekeland IG et. al; Front Med (Lausanne) 2020 Apr 29;7:162. ABSTRACT: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a disease with high symptom burden, of unknown etiology, with no established treatment. We observed patients with longstanding ME/CFS who got cancer, and who reported improvement of ME/CFS symptoms after chemotherapy including cyclophosphamide, forming the basis for this prospective trial. Materials and methods: This open-label phase II trial included 40 patients with ME/CFS diagnosed by Canadian criteria. Treatment consisted of six intravenous infusions of cyclophosphamide, 600-700 mg/m2, given at four-week intervals with follow-up for 18 months, extended to 4 years. Response was defined by self-reported improvements in symptoms by Fatigue score, supported by Short Form 36 (SF-36) scores, physical activity measures and other instruments. Repeated measures of outcome variables were assessed by General linear models. Responses were correlated with specific Human Leukocyte Antigen (HLA) alleles. Results: The overall response rate by Fatigue score was 55.0% (22 of 40 patients). Fatigue score and other outcome variables showed significant improvements compared to baseline. The SF-36 Physical Function score increased from mean 33.0 at baseline to 51.5 at 18 months (all patients), and from mean 35.0 to 69.5 among responders. Mean steps per 24 h increased from mean 3,199 at baseline to 4,347 at 18 months (all patients), and from 3,622 to 5,589 among responders. At extended follow-up to 4 years 68% (15 of 22 responders) were still in remission. Patients positive for HLADQB1*03:03 and/or HLA-C*07:04 (n = 12) had significantly higher response rate compared to patients negative for these alleles (n = 28), 83 vs. 43%, respectively. Nausea and constipation were common grade 1-2 adverse events. There were one suspected unexpected serious adverse reaction (aggravated POTS) and 11 serious adverse events in eight patients. Conclusion: Intravenous cyclophosphamide treatment was feasible for ME/CFS patients and associated with an acceptable toxicity profile. More than half of the patients responded and with prolonged follow-up, a considerable proportion of patients reported ongoing remission. Without a placebo group, clinical response data must be interpreted with caution. We nevertheless believe a future randomized trial is warranted. Clinical Trial Registration: www.ClinicalTrials.gov, identifier: NCT02444091.

* A Systematic Review of Metabolomic Dysregulation in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis/Systemic Exertion Intolerance Disease (CFS/ME/SEID); Huth TK et. al; J Transl Med 2020 May 13;18(1):198. ABSTRACT: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis/Systemic Exertion Intolerance Disease (CFS/ME/SEID) is a complex illness that has an unknown aetiology. It has been proposed that metabolomics may contribute to the illness pathogenesis of CFS/ME/SEID. In metabolomics, the systematic identification of measurable changes in small molecule metabolite products have been identified in cases of both monogenic and heterogenic diseases. Therefore, the aim of this systematic review was to evaluate if there is any evidence of metabolomics contributing to the pathogenesis of CFS/ME/SEID. Methods: PubMed, Scopus, EBSCOHost (Medline) and EMBASE were searched using medical subject headings terms for Chronic Fatigue Syndrome, metabolomics and metabolome to source papers published from 1994 to 2020. Inclusion and exclusion criteria were used to identify studies reporting on metabolites measured in blood and urine samples from CFS/ME/SEID patients

compared with healthy controls. The Joanna Briggs Institute Checklist was used to complete a quality assessment for all the studies included in this review. Results: 11 observational case control studies met the inclusion criteria for this review. The primary outcome of metabolite measurement in blood samples of CFS/ME/SEID patients was reported in ten studies. The secondary outcome of urine metabolites was measured in three of the included studies. No studies were excluded from this review based on a low-quality assessment score, however there was inconsistency in the scientific research design of the included studies. Metabolites associated with the amino acid pathway were the most commonly impaired with significant results in seven out of the 10 studies. However, no specific metabolite was consistently impaired across all of the studies. Urine metabolite results were also inconsistent. Conclusion: The findings of this systematic review reports that a lack of consistency with scientific research design provides little evidence for metabolomics to be clearly defined as a contributing factor to the pathogenesis of CFS/ME/SEID. Further research using the same CFS/ME/SEID diagnostic criteria, metabolite analysis method and control of the confounding factors that influence metabolite levels are required.

* A Systematic Review of Neurological Impairments in Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome Using Neuroimaging Techniques; Maksoud R et. al; PLoS One 2020 Apr 30;15(4):e0232475. ABSTRACT: Myalgic encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS) is a multi-system illness characterised by a diverse range of debilitating symptoms including autonomic and cognitive dysfunction. The pathomechanism remains elusive, however, neurological and cognitive aberrations are consistently described. This systematic review is the first to collect and appraise the literature related to the structural and functional neurological changes in ME/CFS patients as measured by neuroimaging techniques and to investigate how these changes may influence onset, symptom presentation and severity of the illness. Methods: A systematic search of databases Pubmed, Embase, MEDLINE (via EBSCOhost) and Web of Science (via Clarivate Analytics) was performed for articles dating between December 1994 and August 2019. Included publications report on neurological differences in ME/CFS patients compared with healthy controls identified using neuroimaging techniques such as magnetic resonance imaging, positron emission tomography and electroencephalography. Article selection was further refined based on specific inclusion and exclusion criteria. A quality assessment of included publications was completed using the Joanna Briggs Institute checklist. Results: A total of 55 studies were included in this review. All papers assessed neurological or cognitive differences in adult ME/CFS patients compared with healthy controls using neuroimaging techniques.The outcomes from the articles include changes in gray and white matter volumes, cerebral blood flow, brain structure, sleep, EEG activity, functional connectivity and cognitive function. Secondary measures including symptom severity were also reported in most studies. Conclusions: The results suggest widespread disruption of the autonomic nervous system network including morphological changes, white matter abnormalities and aberrations in functional connectivity. However, these findings are not consistent across studies and the origins of these anomalies remain unknown. Future studies are required confirm the potential neurological contribution to the pathology of ME/CFS.

* Autoimmunity-Related Risk Variants in PTPN22 and CTLA4 Are Associated With ME/CFS With Infectious Onset; Steiner S et. al; Front Immunol 2020 Apr 9;11:578. ABSTRACT: Single nucleotide polymorphisms (SNP) in various genes have been described to be associated with susceptibility to autoimmune disease. In this study, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients and controls were genotyped for five immune gene SNPs in tyrosine phosphatase non-receptor type 22 (PTPN22, rs2476601), cytotoxic T-lymphocyte-associated protein 4 (CTLA4, rs3087243), tumor necrosis factor (TNF, rs1800629 and rs1799724), and interferon regulatory factor 5 (IRF5, rs3807306), which are among the most important risk variants for autoimmune diseases. Analysis of 305 ME/CFS patients and 201 healthy controls showed significant associations of the PTPN22 rs2476601 and CTLA4 rs3087243 autoimmunity-risk alleles with ME/CFS. The associations were only found in ME/CFS patients, who reported an acute onset of disease with an infection (PTPN22 rs2476601: OR 1.63, CI 1.04-2.55, p = 0.016; CTLA4 rs3087243: OR 1.53, CI 1.17-2.03, p = 0.001), but not in ME/CFS patients without infection-triggered onset (PTPN22 rs2476601: OR 1.09, CI 0.56-2.14, p = 0.398; CTLA4 rs3087243: OR 0.89, CI 0.61-1.30, p = 0.268). This finding provides evidence that autoimmunity might play a role in ME/CFS with an infection-triggered onset. Both genes play a key role in regulating B and T cell activation.

* Human Herpesvirus-6 Reactivation, Mitochondrial Fragmentation, and the Coordination of Antiviral and Metabolic Phenotypes in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Schreiner P et. al; Immunohorizons 2020 Apr 23;4(4):201-215. ABSTRACT: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a multifactorial disorder with many possible triggers. Human herpesvirus (HHV)-6 and HHV-7 are two infectious triggers for which evidence has been growing. To understand possible causative role of HHV-6 in ME/ CFS, metabolic and antiviral phenotypes of U2-OS cells were studied with and without chromosomally integrated HHV-6 and with or without virus reactivation using the histone deacetylase inhibitor trichostatin-A. Proteomic analysis was conducted by pulsed stable isotope labeling by amino acids in cell culture analysis. Antiviral properties that were induced by HHV-6 transactivation were studied in virus-naive A549 cells challenged by infection with influenza-A (H1N1) or HSV-1. Mitochondria were fragmented and 1-carbon metabolism, dUTPase, and thymidylate synthase were strongly induced by HHV-6 reactivation, whereas superoxide dismutase 2 and proteins required for mitochondrial oxidation of fatty acid, amino acid, and glucose metabolism, including pyruvate dehydrogenase, were strongly inhibited. Adoptive transfer of U2-OS cell supernatants after reactivation of HHV-6A led to an antiviral state in A549 cells that prevented superinfection with influenza-A and HSV-1. Adoptive transfer of serum from 10 patients with ME/CFS produced a similar fragmentation of mitochondria and the associated antiviral state in the A549 cell assay. In conclusion, HHV-6 reactivation in ME/CFS patients activates a multisystem, proinflammatory, cell danger response that protects against certain RNA and DNA virus infections but comes at the cost of mitochondrial fragmentation and severely compromised energy metabolism.

* Altered Muscle Membrane Potential and Redox Status Differentiates Two Subgroups of Patients With Chronic Fatigue Syndrome; Jammes Y et. al; J Transl Med 2020 Apr 19;18(1):173. ABSTRACT: In myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), altered membrane excitability often occurs in exercising muscles demonstrating muscle dysfunction regardless of any psychiatric disorder. Increased oxidative stress is also present in many ME/CFS patients and could affect the membrane excitability of resting muscles. Methods: Seventy-two patients were examined at rest, during an incremental cycling exercise and during a 10-min post-exercise recovery period. All patients had at least four criteria leading to a diagnosis of ME/CFS. To explore muscle membrane excitability, M-waves were recorded during exercise (rectus femoris (RF) muscle) and at rest (flexor digitorum longus (FDL) muscle). Two plasma markers of oxidative stress (thiobarbituric acid reactive substance (TBARS) and oxidation-reduction potential (ORP)) were measured. Plasma potassium (K+) concentration was also measured at rest and at the end of exercise to explore K+ outflow. Results: Thirty-nine patients had marked M-wave alterations in both the RF and FDL muscles during and after exercise while the resting values of plasma TBARS and ORP were increased and exercise induced K+ outflow was decreased. In contrast, 33 other patients with a diagnosis of ME/CFS had no M-wave alterations and had lower baseline levels of TBARS and ORP. M-wave changes were inversely proportional to TBARS and ORP levels. Conclusions: Resting muscles of ME/CFS patients have altered muscle membrane excitability. However, our data reveal heterogeneity in some major biomarkers in ME/CFS patients. Measurement of ORP may help to improve the diagnosis of ME/CFS. Trial registration Ethics Committee "Ouest II" of Angers (May 17, 2019) RCB ID: number 2019-A00611-56.

* Metabolic Dysfunction in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Not Due to Antimitochondrial Antibodies; Nilsson I et. al; Front Med (Lausanne) 2020 Mar 31;7:108. ABSTRACT: Metabolic profiling studies have recently indicated dysfunctional mitochondria in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). This includes an impaired function of pyruvate dehydrogenase complex (PDC), possibly driven by serum factor(s), which leads to inadequate adenosine triphosphate generation and excessive lactate accumulation. A reminiscent energy blockade is likely to occur in primary biliary cholangitis (PBC), caused by anti-PDC autoantibodies, as recently proposed. PBC is associated with fatigue and post-exertional malaise, also signifying ME/CFS. We herein have investigated whether ME/CFS patients have autoreactive antibodies that could interfere with mitochondrial function. We found that only 1 of 161 examined ME/CFS patients was positive for anti-PDC, while all PBC patients (15/15) presented significant IgM, IgG, and IgA anti-PDC reactivity, as previously shown. None of fibromyalgia patients (0/14), multiple sclerosis patients (0/29), and healthy blood donors (0/44) controls showed reactivities. Anti-mitochondrial autoantibodies (inner and outer membrane) were negative in ME/CFS cohort. Anti-cardiolipin antibody levels in patients did not differ significantly from healthy blood donors. In conclusion, the impaired mitochondrial/metabolic dysfunction, observed in ME/CFS, cannot be explained by presence of circulating autoantibodies against the tested mitochondrial epitopes.

* Unravelling Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): Gender-specific Changes in the microRNA Expression Profiling in ME/CFS; Cheema AK et. al; J Cell Mol Med 2020 May;24(10):5865-5877. ABSTRACT: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a multisystem illness characterized by medically unexplained debilitating fatigue with suggested altered immunological state. Our study aimed to explore peripheral blood mononuclear cells (PBMCs) for microRNAs (miRNAs) expression in ME/CFS subjects under an exercise challenge. The findings highlight the immune response and inflammation links to differential miRNA expression in ME/CFS. The present study is particularly important in being

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the first to uncover the differences that exist in miRNA expression patterns in males and females with ME/CFS in response to exercise. This provides new evidence for the understanding of differential miRNA expression patterns and post-exertional malaise in ME/CFS. We also report miRNA expression pattern differences associating with the nutritional status in individuals with ME/CFS, highlighting the effect of subjects' metabolic state on molecular changes to be considered in clinical research within the NINDS/CDC ME/CFS Common Data Elements. The identification of gender-based miRNAs importantly provides new insights into gender specific ME/CFS susceptibility and demands exploration of sex-suited ME/CFS therapeutics.

* Systemic Hyperalgesia in Females With Gulf War Illness, Chronic Fatigue Syndrome and Fibromyalgia; Surian AA et. al; Sci Rep 2020 Apr 1;10(1):5751. ABSTRACT: Pain is a diagnostic criterion for Gulf War Illness (GWI), Chronic Fatigue Syndrome (CFS), and fibromyalgia (FM). The physical sign of systemic hyperalgesia (tenderness) was assessed in 920 women who were stratified by 2000 Kansas GWI, 1994 CFS, and 1990 FM criteria. Pressure was applied by dolorimetry at 18 traditional tender points and the average pressure causing pain determined. GWI women were the most tender (2.9 ± 1.6 kg, mean ± SD, n = 70), followed by CFS/FM (3.1 ± 1.4 kg, n = 196), FM (3.9 ± 1.4 kg, n = 56), and CFS (5.8 ± 2.1 kg, n = 170) compared to controls (7.2 ± 2.4 kg, significantly highest by Mann-Whitney tests $p < 0.0001$, n = 428). Receiver operating characteristics set pressure thresholds of 4.0 kg to define GWI and CFS/FM (specificity 0.85, sensitivities 0.80 and 0.83, respectively), 4.5 kg for FM, and 6.0 kg for CFS. Pain, fatigue, quality of life, and CFS symptoms were equivalent for GWI, CFS/FM and CFS. Dolorimetry correlated with symptoms in GWI but not CFS or FM. Therefore, women with GWI, CFS and FM have systemic hyperalgesia compared to sedentary controls. The physical sign of tenderness may complement the symptoms of the Kansas criteria as a diagnostic criterion for GWI females, and

aid in the diagnosis of CFS. Molecular mechanisms of systemic hyperalgesia may provide new insights into the neuropathology and treatments of these nociceptive, interoceptive and fatiguing illnesses.

* Human Leukocyte Antigen Alleles Associated With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS); Lande A et. al; Sci Rep 2020 Mar 24;10(1):5267. ABSTRACT: The etiology and pathogenesis of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) are unknown, and autoimmunity is one of many proposed underlying mechanisms. Human Leukocyte Antigen (HLA) associations are hallmarks of autoimmune disease, and have not been thoroughly investigated in a large ME/CFS patient cohort. We performed high resolution HLA -A, -B, -C, -DRB1, -DQB1 and -DPB1 genotyping by next generation sequencing in 426 adult, Norwegian ME/CFS patients, diagnosed according to the Canadian Consensus Criteria. HLA associations were assessed by comparing to 4511 healthy and ethnically matched controls. Clinical information was collected through questionnaires completed by patients or relatives. We discovered two independent HLA associations, tagged by the alleles HLA-C*07:04 (OR 2.1 [95% CI 1.4-3.1]) and HLA-DQB1*03:03 (OR 1.5 [95% CI 1.1-2.0]). These alleles were carried by 7.7% and 12.7% of ME/CFS patients, respectively. The proportion of individuals carrying one or both of these alleles was 19.2% in the patient group and 12.2% in the control group (OR 1.7 [95% CI 1.3-2.2], pnc = 0.00003). ME/CFS is a complex disease, potentially with a substantial heterogeneity. We report novel HLA associations pointing toward the involvement of the immune system in ME/CFS pathogenesis.

* Peripheral Endothelial Dysfunction in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Scherbakov N et. al; ESC Heart Fail 2020 Mar 10. ABSTRACT: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a complex multisystem disease. Evidence for disturbed vascular regulation comes from various studies showing cerebral hypo perfusion and orthostatic intolerance. The peripheral endothelial dysfunction (ED) has not been sufficiently investigated in patients with ME/CFS. The aim of the present study was to examine peripheral endothelial function in patients with ME/CFS. Methods and results: Thirty-five patients [median age 40 (range 18-70) years, mean body mass index 23.8 ± 4.2 kg/m2 , 31% male] with ME/CFS were studied for peripheral endothelial function assessed by peripheral arterial tonometry (EndoPAT2000). Clinical diagnosis of ME/CFS was based on Canadian Criteria. Nine of these patients with elevated antibodies against ß2-adrenergic receptor underwent immunoadsorption, and endothelial function was measured at baseline and 3, 6, and 12 months follow-up. ED was defined by reactive hyperaemia index ≤1.81. Twenty healthy subjects of similar age and body mass index were used as a control group. Peripheral ED was found in 18 of 35 patients (51%) with ME/CFS and in 4 healthy subjects (20%, P < 0.05). Patients with ED, in contrast to patients with normal endothelial function, reported more severe disease according to Bell score (31 ± 12 vs. 40 ± 16, P = 0.04), as well as more severe fatigue-related symptoms (8.62 ± 0.87 vs. 7.75 ± 1.40, P = 0.04) including a higher demand for breaks [9.0 (interquartile range 7.0-10.0) vs. 7.5 (interquartile range 6.0-9.25), P = 0.04]. Peripheral ED showed correlations with more severe immune-associated symptoms (r = -0.41, P = 0.026), such as sore throat (r = -0.38, P

= 0.038) and painful lymph nodes (r = -0.37, P = 0.042), as well as more severe disease according to Bell score (r = 0.41, P = 0.008) and symptom score (r = -0.59, P = 0.005). There were no differences between the patient group with ED and the patient group with normal endothelial function regarding demographic, metabolic, and laboratory parameters. Further, there was no difference in soluble vascular cell adhesion molecule and soluble intercellular adhesion molecule levels. At baseline, peripheral ED was observed in six patients who underwent immunoadsorption. After 12 months, endothelial function had improved in five of these six patients (reactive hyperaemia index 1.58 ± 0.15 vs. 2.02 ± 0.46, P = 0.06). Conclusions: Peripheral ED is frequent in patients with ME/CFS and associated with disease severity and severity of immune symptoms. As ED is a risk factor for cardiovascular disease, it is important to elucidate if peripheral ED is associated with increased cardiovascular morbidity and mortality in ME/CFS.

* Cerebral Blood Flow Is Reduced in ME/CFS During Head-Up Tilt Testing Even in the Absence of Hypotension or Tachycardia: A Quantitative, Controlled Study Using Doppler Echography; Linda C et. al; Clin Neurophysiol Pract 2020 Feb 8;5:50-58. ABSTRACT: The underlying hypothesis in orthostatic intolerance (OI) syndromes is that symptoms are associated with cerebral blood flow (CBF) reduction. Indirect CBF measurements (transcranial Doppler flow velocities), provide inconsistent support of this hypothesis. The aim of the study was to measure CBF during a 30 min head-up tilt test (HUT), using Doppler flow imaging of carotid and vertebral arteries, in individuals with chronic fatigue syndrome/myalgic encephalomyelitis (ME/CFS), a condition with a high prevalence of OI. Methods: 429 ME/CFS patients were studied: 247 had a normal heart rate (HR) and blood pressure (BP) response to HUT, 62 had delayed orthostatic hypotension (dOH), and 120 had postural orthostatic tachycardia syndrome (POTS). We also studied 44 healthy controls (HC). CBF measurements were made at mid-tilt and end-tilt. Before mid-tilt, we administered a verbal questionnaire to ascertain for 15 OI symptoms. Results: End-tilt CBF reduction was 7% in HC versus 26% in the overall ME/CFS group, 24% in patients with a normal HR/BP response, 28% in those with dOH, and 29% in POTS patients (all P < .0005). Using a lower limit of normal of 2SD of CBF reduction in HC (13% reduction), 82% of patients with normal HR/BP response, 98% with dOH and 100% with POTS showed an abnormal CBF reduction. There was a linear correlation of summed OI symptoms with the degree of CBF reduction at mid-tilt (P < .0005). Conclusions: During HUT, extracranial Doppler measurements demonstrate that CBF is reduced in ME/CFS patients with POTS, dOH, and even in those without HR/BP abnormalities. Significance: This study shows that orthostatic intolerance symptoms are related to CBF reduction, and that the majority of ME/CFS patients (90%) show an abnormal cerebral flow reduction during orthostatic stress testing. This may have implications for the diagnosis and treatment of ME/CFS patients.

* Cytomegalovirus, Epstein-Barr Virus, and Human herpesvirus-6 Infections in Patients With Myalgic encephalomyelitis/Chronic Fatigue Syndrome; Shikova E et. al; J Med Virol 2020 Mar 4.ncephalomyelitis/Chronic Fatigue Syndrome; Shikova E et. al; J Med Virol 2020 Mar 4. ABSTRACT: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a disabling multisystem chronic disease. The etiology and pathogenesis of ME/CFS are unknown. Infections

of cytomegalovirus (CMV), Epstein-Barr virus (EBV), and human herpesvirus-6 (HHV-6) are suspected as etiological agents for ME/CFS. This study aims to estimate prevalence and type (active/latent) of EBV, CMV, and HHV-6 infections in Bulgarian ME/CFS patients. In the study were included 58 patients with ME/CFS and 50 healthy controls. Virus-specific antibodies were detected by enzymelinked immunosorbent assay and viral genomic sequences in peripheral blood mononuclear cell (PBMCs) and plasma samples by nested polymerase chain reaction (PCR). We did not observe any significant differences in virus-specific immunoglobulin G and immunoglobulin M positivity rates between patients with ME/CFS and control group. In ME/CFS plasma samples, EBV DNA was found in 24.1%, CMV DNA in 3.4%, and HHV-6 DNA in 1.7% of samples. EBV DNA was detected in 4%, and CMV and HHV-6 DNA were not found in plasma samples of controls. The frequency of viral genome detection in PBMCs of patients and controls was 74% vs 78% for CMV, 81% vs 84% for EBV, and 82.8% vs 82% for HHV-6. The difference in frequency of EBV active infection in ME/CFS and control group was statistically significant (P = .0027). No ME/CFS and control individuals with active CMV and HHV-6 infection were observed. In conclusion, this study using both serological and PCRbased techniques for distinguishing between active and latent infection showed high rate of active EBV infection among patients with ME/CFS indicating that at least in a subset of cases, EBV is important factor for the development of disease.

* Cell-Based Blood Biomarkers for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Missailidis D et. al; Int J Mol Sci 2020 Feb 8;21(3):1142. ABSTRACT: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a devastating illness whose biomedical basis is now beginning to be elucidated. We reported previously that, after recovery from frozen storage, lymphocytes (peripheral blood mononuclear cells, PBMCs) from ME/CFS patients die faster in culture medium than those from healthy controls. We also found that lymphoblastoid cell lines (lymphoblasts) derived from these PBMCs exhibit multiple abnormalities in mitochondrial respiratory function and signalling activity by the cellular stress-sensing kinase Target Of Rapamycin Complex 1 (TORC1). These differences were correlated with disease severity, as measured by the Richardson and Lidbury weighted standing test. The clarity of the differences between these cells derived from ME/CFS patient blood and those from healthy controls suggested that they may provide useful biomarkers for ME/CFS. Here, we report a preliminary investigation into that possibility using a variety of analytical classification tools, including linear discriminant analysis, logistic regression and receiver operating characteristic (ROC) curve analysis. We found that results from three different tests-lymphocyte death rate, mitochondrial respiratory function and TORC1 activity-could each individually serve as a biomarker with better than 90% sensitivity but only modest specificity vís a vís healthy controls. However, in combination, they provided a cell-based biomarker with sensitivity and specificity approaching 100% in our sample. This level of sensitivity and specificity was almost equalled by a suggested protocol in which the frozen lymphocyte death rate was used as a highly sensitive test to triage positive samples to the more time consuming and expensive tests measuring lymphoblast respiratory function and TORC1 activity. This protocol provides a promising biomarker that could assist in more rapid and accurate diagnosis of ME/CFS.

* An Isolated Complex V Inefficiency and Dysregulated Mitochondrial Function in Immortalized Lymphocytes From ME/CFS Patients; Missailidis D et al; Int J Mol Sci 2020 Feb 6;21(3):1074. ABSTRACT: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is an enigmatic condition characterized by exacerbation of symptoms after exertion (post-exertional malaise or "PEM"), and by fatigue whose severity and associated requirement for rest are excessive and disproportionate to the fatigue-inducing activity. There is no definitive molecular marker or known underlying pathological mechanism for the condition. Increasing evidence for aberrant energy metabolism suggests a role for mitochondrial dysfunction in ME/CFS. Our objective was therefore to measure mitochondrial function and cellular stress sensing in actively metabolizing patient blood cells. We immortalized lymphoblasts isolated from 51 ME/CFS patients diagnosed according to the Canadian Consensus Criteria and an age- and gender-matched control group. Parameters of mitochondrial function and energy stress sensing were assessed by Seahorse extracellular flux analysis, proteomics, and an array of additional biochemical assays. As a proportion of the basal oxygen consumption rate (OCR), the rate of ATP synthesis by Complex V was significantly reduced in ME/CFS lymphoblasts, while significant elevations were observed in Complex I OCR, maximum OCR, spare respiratory capacity, nonmitochondrial OCR and "proton leak" as a proportion of the basal OCR. This was accompanied by a reduction of mitochondrial membrane potential, chronically hyperactivated TOR Complex I stress signaling and upregulated expression of mitochondrial respiratory complexes, fatty acid transporters, and enzymes of the ß-oxidation and TCA cycles. By contrast, mitochondrial mass and genome copy number, as well as glycolytic rates and steady state ATP levels were unchanged. Our results suggest a model in which ME/CFS lymphoblasts have a Complex V defect accompanied by compensatory upregulation of their respiratory capacity that includes the mitochondrial respiratory complexes, membrane transporters and enzymes involved in fatty acid ß-oxidation. This homeostatically returns ATP synthesis and steady state levels to "normal" in the resting cells, but may leave them unable to adequately respond to acute increases in energy demand as the relevant homeostatic pathways are already activated.

* Assessing Diagnostic Value of microRNAs From Peripheral Blood Mononuclear Cells and Extracellular Vesicles in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Almenar-Perez E et al; Sci Rep 2020 Feb 7;10(1):2064. ABSTRACT: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating multisystemic disease of unknown etiology, affecting thousands of individuals worldwide. Its diagnosis still relies on ruling out medical problems leading to unexplained fatigue due to a complete lack of disease-specific biomarkers. Our group and others have explored the potential value of microRNA profiles (miRNomes) as diagnostic tools for this disease. However, heterogeneity of participants, low numbers, the variety of samples assayed, and other pre-analytical variables, have hampered the identification of disease-associated miRNomes. In this study, our team has evaluated, for the first time, ME/CFS miRNomes in peripheral blood mononuclear cells (PBMCs) and extracellular vesicles (EVs) from severely ill patients recruited at the monographic UK ME biobank to assess, using standard operating procedures (SOPs), blood fractions with optimal diagnostic power for a rapid translation of a miR-based diagnostic method into the clinic. Our results show that routine creatine kinase (CK) blood values, plasma EVs physical characteristics (including counts, size and zeta-potential),

and a limited number of differentially expressed PBMC and EV miRNAs appear significantly associated with severe ME/CFS ($p < 0.05$). Gene enrichment analysis points to epigenetic and neuroimmune dysregulated pathways, in agreement with previous reports. Population validation by a cost-effective approach limited to these few potentially discriminating variables is granted.

* Parasympathetic Activity Is Reduced During Slow-Wave Sleep, but Not Resting Wakefulness, in Patients With Chronic Fatigue Syndrome; Fatt SJ et al; J Clin Sleep Med 2020 Jan 15;16(1):19-28.

ABSTRACT: Physiological dearousal characterized by an increase in parasympathetic nervous system activity is important for good-quality sleep. Previous research shows that nocturnal parasympathetic activity (reflected by heart rate variability [HRV]) is diminished in individuals with chronic fatigue syndrome (CFS), suggesting hyper vigilant sleep. This study investigated differences in nocturnal autonomic activity across sleep stages and explored the association of parasympathetic activity with sleep quality and self-reported physical and psychological wellbeing in individuals with CFS. Methods: Twenty-four patients with medically diagnosed CFS, and 24 matched healthy control individuals participated. Electroencephalography and HRV were recorded during sleep in participants' homes using a minimally invasive ambulatory device. Questionnaires were used to measure self-reported wellbeing and sleep quality. Results: Sleep architecture in patients with CFS differed from that of control participants in slower sleep onset, more awakenings, and a larger proportion of time spent in slow-wave sleep (SWS). Linear mixed-model analyses controlling for age revealed that HRV reflecting parasympathetic activity (normalized high frequency power) was reduced in patients with CFS compared to control participants, particularly during deeper stages of sleep. Poorer self-reported wellbeing and sleep quality was associated with reduced parasympathetic signaling during deeper sleep, but not during wake before sleep, rapid eye movement sleep, or with the proportion of time spent in SWS. Conclusions: Autonomic hypervigilance during the deeper, recuperative stages of sleep is associated with poor quality sleep and self-reported wellbeing. Causal links need to be confirmed but provide potential intervention opportunities for the core symptom of unrefreshing sleep in CFS.

* Comprehensive Circulatory Metabolomics in ME/CFS Reveals Disrupted Metabolism of Acyl Lipids and Steroids; Germain A et al; Metabolites 2020 Jan 14;10(1):34. ABSTRACT: The latest worldwide prevalence rate projects that over 65 million patients suffer from myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), an illness with known effects on the functioning of the immune and nervous systems. We performed an extensive metabolomics analysis on the plasma of 52 female subjects, equally sampled between controls and ME/CFS patients, which delivered data for about 1750 blood compounds spanning 20 super-pathways, subdivided into 113 subpathways. Statistical analysis combined with pathway enrichment analysis points to a few disrupted metabolic pathways containing many unexplored compounds. The most intriguing finding concerns acyl cholines, belonging to the fatty acid metabolism sub-pathway of lipids, for which all compounds are consistently reduced in two distinct ME/CFS patient cohorts. We compiled the extremely limited knowledge about these compounds and regard

them as promising in the quest to explain many of the ME/CFS symptoms. Another class of lipids with far-reaching activity on virtually all organ systems are steroids; androgenic, progestin, and corticosteroids are broadly reduced in our patient cohort. We also report on lower dipeptides and elevated sphingolipids abundance in patients compared to controls. Disturbances in the metabolism of many of these molecules can be linked to the profound organ system symptoms endured by ME/CFS patients.

* Low-dose Naltrexone as a Treatment for Chronic Fatigue Syndrome; Bolton MJ et al; BMJ Case Rep 2020 Jan 6;13(1):e232502. ABSTRACT: Naltrexone is used as an off-label treatment in low doses for several chronic immunemodulated disorders in many countries. Although only small-scale clinical trials have been performed, these suggest efficacy in several diseases including Crohn's disease, fibromyalgia and Gulf War Illness. Despite numerous internet reports of response to low-dose naltrexone (LDN), no clinical trials exist in people with chronic fatigue syndrome. This condition is characterised by chronic profound fatigue, postexertional malaise,

pain and autonomic and neurocognitive disturbances. This series of three case reports compiled by people with long-term ill-health due to chronic fatigue syndrome shows the range of responses they observed when taking LDN, from life changing to a reduction in some symptoms only. Treatment doses ranged from 4 to 12 mg. Clinical trials may be warranted to explore the potential use of naltrexone in people with these debilitating illnesses which currently have no licensed treatments available.

* Reduced Heart Rate Variability Predicts Fatigue Severity in Individuals With Chronic Fatigue Syndrome/Myalgic Encephalomyelitis; Escorihuela RM et al; J Transl Med 2020 Jan 6;18(1):4. ABSTRACT: Heart rate variability (HRV) is an objective, non-invasive tool to assessing autonomic dysfunction in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). People with CFS/ME tend to have lower HRV; however, in the literature there are only a few previous studies (most of them inconclusive) on their association with illness-related complaints. To address this issue, we assessed the value of different diurnal HRV parameters as potential biomarker in CFS/ME and also investigated the relationship between these HRV indices and self-

reported symptoms in individuals with CFS/ME. Methods: In this case-control study, 45 female patients who met the 1994 CDC/Fukuda definition for CFS/ME and 25 age- and gender-matched healthy controls underwent HRV recording-resting state tests. The intervals between consecutive heartbeats (RR) were continuously recorded over three 5-min periods. Time- and frequency-domain analyses were applied to estimate HRV variables. Demographic and clinical features, and self-reported symptom measures were also recorded. Results: CFS/ME patients showed significantly higher scores in all symptom questionnaires ($p < 0.001$), decreased RR intervals ($p < 0.01$), and decreased HRV time- and frequency-domain parameters ($p < 0.005$), except for the LF/HF ratio than in the healthy controls. Overall, the correlation analysis reached significant associations between the questionnaires scores and HRV time- and frequency domain measurements ($p < 0.05$). Furthermore, separate linear regression analyses showed significant relationships between self-reported fatigue symptoms and mean RR ($p = 0.005$), RMSSD ($p = 0.0268$) and HFnu indices ($p = 0.0067$) in CFS/ME patients, but not in healthy controls. Conclusions: Our findings suggest that ANS dysfunction presenting as increased sympathetic hyperactivity may contribute to fatigue severity in individuals with ME/CFS. Further studies comparing short- and long-term HRV recording and self-reported outcome measures with previous studies in larger CFS/ME cohorts are urgently warranted.

HOW DID I GET RADIATION POISONING?

Nobody really will ever know for sure just how they got ionizing radiation that has caused them to have ME/CFIDS. There's no taste or smell nor can one hear or see ionizing radiation. Ionizing radiation comes from natural sources such as soil or rocks or even cosmic rays. Of course, there's also other sources where it is produces via medical or even industrial processes. There is absolutely no dose that is safe and women and children are at higher risk than are adult males. That's probably why ME/CFIDS affects more females but men can get it and their dose can make them as sick as females.

You may have eaten some contaminated food or breathed in some air that was contaminated. When this happens, your own body doesn't recognize that a radionuclide isn't a natural element. When this occurs, it can lodge in your muscles or your bones and becomes internal radiation. Once they are inside, these radionuclides can attack your organs. Nuclear accidents, like Chernobyl and Fukushima, last millions of years and have spread around the entire world. There are also naturally occurring radionuclides that can inhabit the body naturally although they are usually at low levels and is called background radiation. This is not harmful but the additional radiation that has come into your body is able to radiate for a long time. Those patients that have absorbed a smaller dose will not have as severe a reaction as those that absorbed a higher dose. There is not any dose that is considered safe.

CHESHIRE CAT SMILE

By Ken Kansky – Copyright 2020

I dream for you even bigger than me. For right just now I can barely see where I will land.
No way to realize which way is forward in burning dust of sand dunes shifting…

To those I have left behind. I question where you have been right over time.
Was I too crazy or not enough fun to see the light and love in me.

Those late nights I crave where the stars shine a fine line between the heavens and the fade.
I dream of legal crimes of happiness and fun with an outdoor club bass laser beat.

Adventures of exploration ruins and sun with palm trees protecting the bright light from my chair.

The world is open and although my dream to scuba dive again is lost for now…the turquoise water will again lap the lagoons of my future.

I seem to know I will be just ok. Where has my confidence gone. I can think outside the box. Especially this one. I will save money and roar to the top. No weight belt will keep me down. I have enough altitude to stay aloft even with bad actors lying their way to make my tiger leap stop.

If I can focus on being clever from the best who hone the craft. If I can just pretend I'm in the same air of which I am. There is only one breakfast truck on a set. And the full catered lunch was not built just for me. Included free of charge for the cast and crew. I see you….do you see three. Or have I already worked for your studio too, just smaller parts no one really knew. Subliminal me or Disney. I'm now almost licensed to sell you property.

I won't stop there with logistics too. I'm a talented writer just for you. Because my looks are blue collar and my mind is stellar with just enough sleep to precision drive forever. Dream my dreams and I'm sure to win. The games are not over if I just begin. Watch my solar top spin the dial I rinse and repeat with my Cheshire cat smile.

PAIN

Do you have pain? Dr. David Nierman, a professor from the Appalachian State University in North Carolina, found that bicyclists who ate bananas during their bike rides had reduced inflammation. It seems as if the antioxidants and other nutrients in bananas are helpful.

Will a baby aspirin a day keep heart disease away? It's a myth! Two huge trials taken fairly recently found a low-dose aspirin did not prevent a first heart attack or stroke but it did increase the risk for gastrointestinal bleeding and increased cancer deaths in both trials. If you've already had a heart attack, a daily low-dose aspirin is recommended.

Aculief is a fairly new device that is used to reduce pain according to the manufacturer who claim their "gadget solves chronic pain instantly". It is drug free, wireless and lightweight. If you have tried Aculief, please let us know about your experience with it as soon as possible via phone or letter. An article that you write about it will be welcomed.

READING ABOUT CFIDS/ME AND GAINING PERSPECTIVE

By Alan Cocchetto – Copyright 2020

As a longtime patient, I love to read. As such, I consider myself very fortunate to be able to do so daily. Usually my reading is both technical and medical but every now and then I stumble upon a real gem… something that moves me to the very core of my being. I am referring to an authentic and sincerely written blog on the internet for all fellow patients to read to gain insight not only into their disease but perhaps their personal lives and daily outlook as well.

Many months ago, I happened to be surfing the web one evening and I ran across a ME blog titled "A Life Hidden" which can be found on the web at "alifehidden.com." This blog is written by Naomi Whittingham, a severe thirty-year ME patient who lives in the UK. Naomi has had ME since her early teen years and she has had her share of health challenges. Her blog is dedicated to those who are shut away from the world because of the intense suffering of severe ME. Her writings serve as a terrific resource for those who wish to learn more about this disease and include a collection of her advocacy work. From my own personal perspective, she is truly a magnificent writer who in spite of her illness and physical limitations, uses her voice to speak for those who cannot. In my mind, she is a true blessing and champion for all patients worldwide. Her many gifts are most apparent in her writing. Some of Naomi's recent blog topics include:

* Severe ME Left Me In a World of Pain and Darkness
* Glimpsing the World: My Joy and Pain
* The Power of Listening
* Life in Lockdown: What Matters When All Is Lost

My brief review here is meant to provide the patient community with a notification that this beautifully written and expressive blog exists for the betterment of each and every one of us with this disease. My hope is that you will take the time to visit and to explore her wonderful blog on the web.

ERRONEOUS NEWS VS FACTS

By Retired LPN Nurse, Diana Saba

TY M. P.

"From California to New York Island...

This...

Was made for you & me...

ME

Statins...

Weakens muscles...

What is a 🤎 ?

Voice's from Ghetto's...

Go to sleep WHO...

Corporations...

Oops, meant

Corruption knowingly...

Erroneous diagnosing...

To be continued?

Gitmo turn your speakers up...

America...

My Country Tis Of Thee...

Time to detox?

Military dot com...

Check your media sources...

Outlets...

And, so...

Online WACOC News...

Hips boots on...

Prayer's...

Standing tall...

Now I lay me down to sleep...

He..

Can turn the tide...

And...

Calm...

The angry sea.

Until...

FORUM FEEDBACK

"I can't tell you how much I enjoy the Forum. I must reread it dozens of times!"

-M.R., California

"...I remain hopeful and determined beyond measure. I'll never stop persevering. I'm just half dead as well but my human spirit is limitless...the Forum is outstanding..."

-S.O., New York

"...and one of the best articles I read was 'Anesthesia and Advancements'. I've talked to a few patients who only had this horrid illness for a few years and they never heard of the wonderful researched facts that were discovered. As the author pointed out, it is really upsetting that they haven't researched what they've been diagnosed with..."

-R.L., South Carolina

"...And please thank the author who wrote about how to get paid for caregiving. I wish I had known about this quite a few years ago but it will make the future a bit easier. The Forum sure knows how to give us a lot of help even though a treatment is not yet available. I hope the enclosed donation is helpful."

-Anon., Ohio

"I showed my doctor the Forum with the article about the physician who commented about radiation and he asked to borrow it. That was in January and I just got it back in the mail today! Wow!! He told me that he subscribed!"

-H.W., Maine

"...And please let the author of 'Ask Bernie the Attorney' know that his information helped me get the benefits that I was entitled to receive. I belong to a patient group that meets to discuss our lives with this illness and the ones that were not already members of the NCF said they'd join! Thank you all so much."

-J.A., Virgina

"Thank you and all your wonderful helpers for all your years of hard work in keeping us informed."

-T.S., Washington

"I read every word of the winter edition of the Forum as I have with every edition since the mid-1990's. I'm still here, still making the best of each day and remain so very thankful for all the NCF has and continues to do for people with CFIDS/ME! A special thank you to Dr. Alan Cocchetto for his tactful and thorough response to the physician who challenged the validity of radiation as the cause of CFIDS/ME. It gave me the opportunity to review the research findings funded by the NCF. I look forward to research findings on treatments that may help CFIDS/ME people around the globe."

-J.L., MSHP, BSN, RN Retired, TX

"WAY TO GO COCCHETTO in response to question in Forum!!! Thank you! I became very ill on my third day while visiting friends in Krakow, Poland in March 1996. Krakow is only 460 air miles from Chernobyl to the west. I have never been the same since..."

-P.J., Wyoming

"THE TRUTH ABOUT WIRELESS PHONES AND WIRELESS RADIATION"

The title of this article was the title of a lecture given by Dr. Devra Davis at the University of Melbourne in Australia and is available today on YouTube. Dr. Davis got her PhD and another masters in the U.S. from the University of Chicago and Johns Hopkins and, in 2007, formed a nonprofit. Her talk was mainly on wireless phones but also included information on all wireless electronic devices and their dangers of radiation. She is working with Yale on the problem of how to protect pregnant woman and children from mobile phones. Many countries have stated precautions on using mobile phones such as India, France, Canada and Israel but the U.S. is not funding any research in this area despite a 2014 U.S. District Court Ruling to study mobile phones.

Mobile phones can give you exposure to radiation. Even microwave ovens use the same spectrum but they differ in power. It is the pulse, not the power, that gives power density. Keeping wireless phones in your pants pocket is dangerous as it can lead to the exposure of radiation to the groin and bone marrow. Keeping it in your jacket pocket can expose you to radiation of the breast and that goes for men as well as women.

Mobile phones, of course, aren't the only problem regarding radiation. Even UV light from the sun is a problem. UV light through the eyes and nose goes into the brain. Smaller adults get more UV radiation as well as children but a professor who let the United States know about this was not allowed, by our own Centers for Disease Control and Prevention, to show the radiation dose that is given in this way.

NATO worked on this and discovered the radar ranges that are now called microphones. They studied animals that had been exposed and found damages to their livers. The animals that were exposed as newborns shared damage to the brain. Newborns that were exposed in Australia had impaired memory and learning problems. More pediatric cases in the U.S. and India that were studied had damage to the sperm. The Cleveland Clinic found sperm counts were lowered causing fertility problems. Lowered testosterone is found in both men and women.

Mobile phones are now used in schools. In India, no WIFIs for children are allowed in India and none are allowed in kindergarten in Israel and Canada. All these facts can be found on YouTube and, back in 2015, the number of those who went to this site to see these facts numbered 1,213,382 views!

GETTING THE RIGHT DIAGNOSIS

By Kathy Collett

Over the decades, I have met many ME patients and felt an instant connection when discussing symptoms and sharing experiences. On the odd occasion, I have met others who have said they have ME but I have felt they were talking about completely differently illnesses and I could not connect to their situation. While I felt they were ill, they definitely did not sound like we were inflicted with the same illness.

As a long-term patient, I have seen the perception of the illness change from when I was diagnosed decades ago. There are overlapping conditions attached to ME and, in my case, I have Fibromyalgia and Repetitive Strain Injury which Dr. Jay A. Goldstein recognized as overlapping (they all involve brain dysfunction). More than a decade and a half later, some lay people have tried to reframe ME and have added on other unrelated illnesses/conditions such as CCI (cranial) which required an operation and was successful for Jen Brea, maker of the film, Unrest. She had structural problems.

With the absence of a diagnostic test, people presume they have ME. Unfortunately, CCI and ME are not associated and this leaves some new patients baffled. This led to a discussion I had on Twitter with Jen Brea when she started off a conversation. It went like this:

JB: We have no way of clinically distinguishing under current practices between a CCI (cranial) patient and an ME patient with undiagnosed CCI (None. Until we study this, we have no idea. Truly).

KC: I think it is possible using tests CD2, CD4 etc. as I have mentioned before. Also, Dr. Heng found damaged chromosomes in ME patients using SKY technology, which was invented in Australia and, he said, "Previously it wasn't possible to conduct such tests". Then there's CD2, CD4 etc. Immune tests and ME is transgenerational. Not to forget cell damage. All those tests separate ME from other illnesses.

JB: There have also been so many unelicited findings of specific agents/infections etc. usually found by a single researcher or clinician. Most of them are observational/correlative findings. This makes them difficult to interpret.

KC: Prof Hokama was recognized as a leader in the field of ciguatera epitope (toxins) and his anesthesia protocol was published in a medical journal. He found ME research so interesting that he put off retiring.

Later she added:

JB: This is not a difference between ME and CCI patients. Most patients who have CCI because they have ME, EDS and/or MCAS (these are conditions she uses to reframe ME) also have special anesthesia needs. But no, they aren't risking death because of a hypothesized mitochondria problem.

Obviously, an operation will not cure ME or repair damaged cells or damaged chromosomes identified by research funded by The National CFIDS Foundation. Jen Brea was operated on and her situation changed. A few weeks after my Twitter conversation, Dr. Guthridge, an Australian doctor who has the illness, noted that patients are self-diagnosing their illnesses. He tweeted the following:

"Here's the problem with ME/CFS: 70% of people with ME/CFS symptoms cannot get a diagnosis and, in desperation, end up self-diagnosing. But what if they didn't have #MECFS? What if their illness simply mimics some ME/CFS symptoms and what if their illness was treatable?"

My reply to his tweet was:

"Misdiagnosis and/or self-diagnosis is a problem. I heard of someone who self- diagnosed ME and had thyroid problems. Likewise, some doctors focus on fatigue and diagnose depression ignoring the organic issues. Fatigue is associated with cancer and other illnesses." pwME #MyalgicE

Following my response above, Dr. Guthridge did some research and tweeted the following:

"Low blood calcium and PTH levels are used to diagnose hypothyroidism. Patients must have skull thickening with increased risk of neck vertebral abnormalities. Can be treated with #Vitamin D, calcium and sometimes with the PTH. (nature.com/articles/nrdp2)"

Gail Kansky, Editor/President of The National CFIDS Foundation, told me the following tests apply to ME:

There should be irregular results via tests CD3 total lymphocytes, CD4 helper T cells, CD8 cytotoxic/suppressor T cells and CD19 mature B cells. Also Kappa/Lambda Light Chains and Soluble IL-2R show disability scores.

Ed. Note: Kathy is from Australia and her twitter is @kathycollett7.

CORONAVIRUS AND CFIDS/ME

Covid-19 has presented a special problem for patients who have CFIDS/ME since they already have a lowered immune system which make it easier for the virus to invade their lives. Of course, the key preventative measures for avoiding the virus that has become a pandemic remain the same: keep surfaces clean, thoroughly wash hands and wrists after touching any surface away from home, don't touch your face, keep a safe distance from all people and avoid anyone who may any signs of infection. For patients who are mobile and can leave home, the extent of how much they distance themselves from others must be an individual decision.

Each patient must decide on their own if visitors to their home should be restricted and alternative measures put in place such as telephone calls as well as what regular shopping should be changed to home deliveries. All patients with this illness who are not housebound should consider how to reduce their social mobility. Any viral infection can cause symptom exacerbation and relapse of CFIDS/ME so all PWCs should err on the side of caution.

It has been shown that the coronavirus can last for weeks. One PWC that caught it had extreme difficulty breathing as well as fever, chills and exhaustion. She remembered the person she probably caught the virus from yet she felt no effects of it for well over a week. Another was in an ICU at a local hospital for weeks.

It's bad enough dealing with CFIDS/ME. Having to cope with covid-19 as well is far worse. We hope the PWC reading this will not have to deal with that virus in addition to their disease. If it continues to be difficult for those who are healthy to deal with the coronavirus, it's far, far harder to deal with if one is not well. If they are living with CFIDS/ME, it is even more difficult

as few have doctors that are knowledgeable about ME since it has not been taught in medical schools in the U.S.

ASK BERNIE THE ATTORNEY

By Bernard A. Kansky – Copyright 2020

Q. Now that we are subject to the Corona Virus pandemic, when applying for Social Security Disability Benefits, also known as SSDI, is there anything more we should do to improve our chances for a successful finding of totally disabled now that
even victims of the Corona Virus, who have generally "recovered," may have some severe residual lingering symptoms which could qualify them also as **totally disabled**, especially if their residual symptoms are severe enough to prevent them from returning to their usual or other regularly scheduled, gainful employment activity.

A. Yes. Before allowing any evaluation by SSA.s physicians, occupational therapists and even regular office staff working the local SSA offices, be certain to have first provided the local office staff with detailed medical reports verifying the one or more bases for a determination by your own treating physicians that you are clearly unable to engage in any gainful employment activity which includes even light sedentary activity, from the actual onset date from when you were first unable to work regularly to the present and for the foreseeable future but in any event for not less than the next 12 consecutive months or more. Frequently when ME patients first become disabled, they believe that it is temporary and when they believe they are feeling a little bit better will attempt a return to work. However, that attempt is frequently erratic with hours or days lost from work inasmuch as the patient is unwilling at first, to accept the fact that he or she might be totally disabled. When the testing arranged by the treating physician(s) including but not limited to a detailed testing and review by a well-respected and well known occupational expert and especially one who previously and/or currently provides opinions to Social Security staff and physicians, along with written test results from your own exercise tolerance testers which prove that when undergoing exertion, you use more oxygen than you are able to replace, and that after such exertion, you are so overwhelmingly dysfunctional, you are then clearly not a candidate to perform any gainful employment activity on any regularly scheduled basis i.e. 8 hours a day, 5 days a week, week after week, even for light. sedentary work activity. What is frequently withheld by many patients is the fact that they must always have quick and easy access to a nearby bathroom, or they will experience embarrassing accidents. Yes, there are embarrassing accidents and yes, they are embarrassing to disclose to doctors, SSA staff and Administrative Law Judges, but if truthful and when combined with other medical and vocational tests and reports, what stronger evidence can exist to prove absolute and total disability from performing gainful employment activity.

If any questions and if you are not already represented by counsel, please forward any such questions to ASK BERNIE The Attorney c/o The National CFIDS Foundation, Inc., 103 Aletha Road, Needham, MA 02492-3931

LAMENT OF THE LIVING DEAD

By Rosie Bayman

Trapped forever within our homes,

And then confined to bed.

We know only darkness –

We are the living dead.

The world it has forgotten us,

And life's been unforgiving.

We can only wait in pain –

We are the dead, living.

We fear more degradation

Is all that lies ahead:

We know we must submit to it –

And continue living dead.

A grief flowers within us

At how the years have sped,

With no relief or end in sight –

Only ever living dead.

A grief flowers within us

At how the years have sped,

With no relief or end in sight –

Only ever living dead.

We spend our lives imagining

The lives we may have led,

If life had not abandoned us –

And left us living dead.

NEWS BITS

On January 21, an expose in Rolling Stone told of how wastewater from many gas and oil wells is dangerously radioactive. The PSR (Physicians for Social Responsibility) held a webinar with the reporter who investigated and wrote about that information and reported, "A sweeping arc of (radioactive) contamination – oil-and-gas waste spilled, spread, and dumped across America..."

Dr. Soumya Swaminathan, M.D. is the Chief Scientist of the World Health Organization (WHO) put out a public service announcement in April that included her saying, "Vaccines are very safe" and that they can "prevent disease without risks." However, there was a leaked vaccine summit of the WHO where Dr. Swaminathan said, "We really don't have very good safety monitoring systems...(we) learned about adverse events only after the drug's been licensed and introduced into the population. So I think that risk is always there..."

In April, Beyond Nuclear International wrote, "The coronavirus killed the Tokyo 2020 Olympics, or at least postponed them. But the radiation levels should have." The Fukushima nuclear disaster left lingering hotspots of radiation. They also felt the United States should "wash our hands of nuclear weapons" as they told how the United Kingdom was ready to buy new nuclear weapons that were being developed in the United States.

As Covid-19 was spreading in April, the problem of workers becoming sick who worked in the nuclear power industries in the United States was evident. The CDC advised the Nuclear Regulatory Commission to put into place "social distancing" at all reactor sites to help protect them from the coronavirus. What would protect them from radiation?

Firefighters in Vinnytia, Ukraine were struggling in April to contain wildfires that were burning in the radioactive forest around the Chernobyl nuclear plant. Meanwhile, nuclear plant employees are considered essential workers in the United States. Thousands of them came down with the coronavirus infection.

On the first day of May, the Countess of Mar retired from the United Kingdom's House of Lords. She had served for 45 years and voted against the PACE trial as well as speaking out against Dr. Wesseley, who was an advocate of exercise to help ME/CFIDS patients. Truly, she was a real Parliamentary champion.

Erratum: In the poem, "The Unhonored", by Richard Fye, the work "unsolhable" should have been "unsolvable".

IN MEMORIAM

The following names have been added to our Memorial List available at our website: http://www.NCF-NET.org. Our sincere condolences to the friends and families of all those on our Memorial List.

Rosie (Rose Mary) Bayman was bedbound with ME for 5 years before she died in 2018. As she lay in silence and in darkness, she made up poetry in her mind and use a recorder. Rosie lived in Warwickshire, England and often offered her poetry on twitter where many enjoyed her humor and warmth. (Further information welcomed) Darden Burns, 65, took her own life after suffering with ME since she was in college. Darden was a talented singer as well as a guitar player and pianist who taught piano and directed a concert series. She grew up in the northeast but, when married, moved to an island off Washington state and enjoyed hiking, and gardening as well as teaching music. After careful researching, she tried various methods of treatment but found none helpful. She is survived by her husband, Michael, two daughters and one grandchild as well as her brothers.

Rose-Marie McGinn died in her native country of England in early 2020 after suffering for years with CFIDS/ME. She worked in the clerical medical field. (Further information about her is welcomed.)

Cindy Siegal Sheplar, 62, died on December 16, 2019. She had ME before she was a teenager in Knoxville, Tennessee. She graduated summa cum laude from San Francisco State University. She married Dave but decided to have no children as she didn't want to pass her illness on. She became an advocate. Less than a decade before her death, she developed a genetic disorder and depression. Cindy's demise left her relatives and friends with deep sorrow as they remember her and the many wonderful things she did despite suffering with her illness.

Marcie Lynn Zinn, Ph.D., 68, died in a Chicago hospital on December 28th, 2019 of sudden heart failure. Diagnosed with CFIDS/ME in 2009, she joined Stanford Medical School's CFS Initiative where her goal was to study cognitive impairment and neurological issues. Her work may lead to treatments in the future. She is missed by her husband, Mark, along with her brother and many friends and colleagues. She is also missed by the many animal pets she owned including a bird, several cats and a service dog.

DONATIONS

The National CFIDS Foundation is immensely grateful to each person listed below. Every penny of their donation has gone to fund research that will eventually help us all live our lives better than ME/CFIDS has allowed thus far. Each donation to the NCF is tax deductible to the full extent allowed by US federal law as our charity is a federally approved 501(c)(3).

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Thank you

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