Guildford ME/CFS Support Group
(& West Surrey)

Newsletter

September 2020

Future dates

Due to the Covid-19 Pandemic we are unable to offer monthly meetings until further notice.

Active Epstein-Barr infections found in large ME/CFS study

Source: www.prohealth.com/me-cfs/library/active-epstein-barr-infections-found-in-large-me-cfs-study-94325
24th July 2020

A Bulgarian team (on behalf of the European Network on ME/CFS (EUROMENE)) assessed the prevalence of latent and active Epstein-Barr, cytomegalovirus and human herpes virus 6 in 108 ME/CFS patients and healthy controls (58 ME/CFS; 50 healthy controls).

Besides being larger than many past studies, this study went a step further than most past studies. Most studies have relied on more indirect measures such as antibody tests that assess whether an immune response has been raised to determine whether active herpesvirus infections are present. This study, though, assessed antibodies and used a process called PCR to directly look for signs of herpesviruses (herpesvirus DNA) in the plasma.

While several EBV antibody studies have had conflicting results, I was able to find only published two studies that have assessed active EBV infections using PCR. Neither found evidence of active herpesvirus infections in ME/CFS. One, however, was very small (n=20) and the other was 20 years old. In 2013, though, Ian Lipkin reported in a CDC talk that he failed to find direct evidence of herpesvirus infection in almost 300 people with ME/CFS.

If pathogens are in a latent state they should remain in the cells and not be present in the blood. Almost all of us carry latent or inactive herpesvirus infections in our cells. They are not a cause for alarm. Active herpesvirus infections, in which the pathogen is actively replicating and spreading from cell to cell through the blood, are another matter.

Results
The study did not find evidence of increased active cytomegalovirus or HHV-6 infections in the ME/CFS group. Two findings, however, suggested that active EBV infections – perhaps similar to those found in infectious mononucleosis/glandular – were significantly more prevalent in the ME/CFS group.

Almost 25% of the plasma samples from ME/CFS patients were positive for EBV DNA. Almost 2/3rds of those patients also had high levels of antibodies (EBV-CA IgG class antibodies) that have been linked with active infections. (This type of antibody latches onto an antigen on the capsid or shell of the virus. These particular antibodies fade quickly after the virus is vanquished from the blood.)

The study didn't find evidence of active HHV-6 or CMV infections. (Some researchers, however, believe that a smouldering infection that this type of research wouldn't detect may present in a subset of ME/CFS patients. Also low level HHV-6 infections in the organs may not show up in the blood. Nor did the study assess the early EBV proteins that Williams at Ohio State University has been finding in ME/CFS.)

Using both serological tests and PCR, this study provided a robust finding of an active EBV infection in about 20% of the ME/CFS patients tested. The authors asserted that this finding indicated "EBV is an important factor for the development of the disease" in at least a subset of patients.

For the full version of this article please refer to the link provided as the source earlier.

Are Covid-19 studies already providing clues for ME/CFS?

Source: www.healthrising.org/blog/2020/08/15/covid-19-sars-cov-2-clues-chronic-fatigue-long-haulers

By Cort Johnson 15th Aug 2020

Two articles in the New York Times – a feature length one, "How Covid Sends Some Bodies to War With Themselves", and "Scientists Uncover Biological Signatures of the Worst Covid-19 Cases" – present the possibility that it is.

Cytokine storms (a very imprecise term) and a tricky immune system are at the heart of it. The feature New York Times piece starts with Dr. Iris Navarro-Millán, a New York rheumatologist who had just watched the health of a 61-year-old COVID-19 patient with mild shortness of breath suddenly plummet. Despite being given oxygen, he'd ended up on a ventilator and requiring dialysis for two months.

Some doctors are using immune suppressants like Anakinra to combat cytokine storms in COVID-19. Navarro-Millán concluded that a cytokine storm had wiped his lungs and kidneys out. She'd seen this kind of thing before in autoimmune patients experiencing a sudden flare. The proper response was simple – knock the immune system down with steroids or other drugs.

COVID-19 patients, though, were fighting off an infection. The accepted wisdom was that tamping down the immune system during an infection would make things worse. Nevertheless, Navarro-Millán tried something different in the next COVID-19 patient showing signs of a rapid decline – a quick-acting immune-suppressing drug called Anakinra.

The patient rapidly got better. In June, Navarro-Millán published a small (n=14) case series report suggesting that Anakinra may have helped prevent mechanical ventilation in about half of the patients. Anecdotal reports from Italy and from several hospitals in the U.S, suggest that glucocorticoids and other immune-suppressing drugs have been helpful. As soon as they see oxygen levels drop, they provide them. Clinical trials are needed, however, to validate her findings.

An Anakinra ME/CFS study unfortunately failed, but in that study Anakinra was given long after initial infectious event occurred.

If Navarro-Millán is correct, though, antiviral drugs like Remdesevir, that one would intuitively think would be beneficial, will have limited effects in some patients. Studies suggest that Remdesevir does accelerate recovery times, but does not significantly affect mortality; i.e. if you were going to be able to fight off the virus, Remdesivir could help you do that more quickly.

If, on the other hand, if your immune system had turned on you and a "cytokine storm" was the problem, it doesn't significantly help.

The studies suggest that the people who are dying from COVID-19 may not be dying from the virus – they're dying from the cytokine storm their bodies have initiated in an attempt to fight off the virus. If that's true – and it's still a hypothesis – effective COVID-19 treatment will depend on identifying just what kind of COVID-19 patient you are – do you need pathogen suppression (or immune enhancement) or immune suppression?

One major study of almost 6,500 patients provided hard evidence that immune suppression was the ticket for some. It found that low to moderate doses of a steroidal, immune-suppressing drug called dexamethasone reduced death rates by a third. Here was solid evidence that in some cases, immune suppression worked.

Of course, it wasn't as simple as giving everyone the drug.

Timing is everything

After noting that dexamethasone was cheap, widely available and safe, a published comment on that study, titled "After 62 years of regulating immunity, dexamethasone meets COVID-19", concluded that "timing was everything" with the drug.

The "cytokine storms" don't happen with everyone. People who are able to mount a strong early immune response to the virus may never experience one. Oddly enough, it's the people who can't amount a strong early immune response who may get plastered by a cytokine storm later. At that point – apparently alarmed by all the damage present – they go into overdrive.

The authors believe that the appearance of substances called "alarmins", which are associated with cell damage caused by the pathogen, sends the immune system into hyperdrive, resulting in inflammation and even more cell damage. An uncontrolled, positive feedback loop then occurs as inflammation-induced damage triggers more inflammation, leaving the COVID-19 patient in real trouble.

The authors proposed that the best course before the alarmins show up is to try and fight the virus off. After they show up, though, immune suppression is needed.

It gets more complicated. Many types of immune responses may show up – each with an optimal treatment protocol.

Subtypes
In "Scientists Uncover Biological Signatures of the Worst Covid-19 Cases", Katherine Wu of the New York Times reports that the immune systems of some people with COVID-19 appear to have trouble marshalling the right kind of immune response. In a massive, but largely fruitless effort, their immune systems are spraying bullets all over the place – but missing the target. (A similar process has been suggested in ME/CFS).

In fact, one study suggests that these dysfunctional immune systems appear to have been tricked into mounting an immune defence more suited to bacteria and fungi than viruses. The immune system's misguided efforts leave the virus intact and a long-term immune response stuck on the on-button.

Adequate early immune response to the virus – Interestingly, the dexamethasone study found that the drug actually made people with mild cases of COVID-19 worse but did not increase their mortality rates. This suggests that if your immune system is already successfully fighting off the virus, you don't need dexamethasone.

Poor early immune response to the virus – People with an insufficient early innate immune response (people who are older or who have immune issues) may suffer later when their immune system finally gets into gear and then compensates by going into hyperdrive – flooding the body with cytokines and causing a vicious cycle of inflammation-induced damage to occur.

These people may need to get their immune or antiviral response boosted early in order to avoid a cytokine storm that comes later. Because immune responses will vary, identifying and then boosting the specific immune deficiency they have would be the most effective.

People in the throes of a cytokine storm – these people need immune suppression. Broad spectrum immune suppressants such as dexamethasone can be helpful, but a more precise reading of the immune system could allow doctors to target the specific part of the immune system that has overheated and tamp that down.

The inability to distinguish immune subsets may explain why immune suppression appeared to fail to work with the first coronavirus that appeared in 2003, or in sepsis. In two cases, researchers who have gone back and re-analysed old trial results have found that immune suppression did work – but only in those patients whose test results suggested they had high levels of inflammation.

Clues for ME/CFS and the long haulers?
With many immune drug trials underway, we should learn much more about their impact on COVID-19. Early into the pandemic, though, without the results of any long-hauler studies published, we may be getting some clues as to what may have gone wrong very early in the disease process in ME/CFS and the long haulers.

People with initial poor responses to the virus may have set themselves up for a devastating cytokine storm later – which could then set the stage for a prolonged illness. Ron Davis has said that he believes the damage that sets ME/CFS in motion probably begins very early – hence his desire to get a hold of coronavirus patients very early in the game.

While the Dubbo studies may not have tested their participants early enough to catch that, they represent a landmark effort to understand what happens in post-infectious illness. They tracked an extensive cohort of people (n=253) who'd experienced various infectious events (Ross River virus, Epstein-Barr virus, Q fever (Coxiella burnetii) over the course of year in the mid-2000's. All

appeared to have been successfully treated for the pathogen they'd encountered; i.e. testing suggested it had been vanquished.

They found, though, that 35% of people still had "post-infectious illness" (e.g. chronic fatigue syndrome) at 6 weeks, 27% did so at three months, and 9% were still sick at 12 months. The studies also found that while the initial symptom set was different in all three infections, it evolved over time to a general pattern characterized by fatigue, musculoskeletal pain, and neurocognitive issues.

The study found that more severe symptoms early were associated with an increased risk of coming down with a post-infectious illness. That could suggest a hyperactive immune response (cytokine storm?), which set off a strong case of "sickness behaviour".

That finding was buttressed a bit by a genetic study which found that small changes (single nucleotide polymorphisms (SNPs)) in two immune genes involved in the early immune response were associated with an 8-fold increase in a person's chance of having a "severe illness response"; i.e. ME/CFS.

Increased incidence of a SNP which boosts interferon gamma (IFN-y) was especially intriguing because IFN-y administration has been show to produce the array of symptoms associated with an infection; i.e. "sickness behaviour". Similarly, the over-representation of an IL-10 SNP, which muffles its anti-inflammatory effects, might set the stage for an early heightened immune response.

While the study never found direct evidence on increased cytokine levels, cell cultures confirmed that people with these SNPs did indeed produce more pro-inflammatory cytokines. That finding sent the authors were looking not to the body but to the brain. They believed that an active cytokine response early in the illness tweaked the microglia to sensitise central nervous system pathways and produce ME/CFS.

That's an interesting conclusion given that some COVID-19 researchers are already tentatively linking cytokine storms to central nervous system dysfunction. They believe it may be possible to identify cytokine profiles that are likely result in long term central nervous system issues and use anti-inflammatories or other drugs to knock them down.

The fact that the genetic polymorphisms identified appeared to have the same effect on each of the infections was striking and left the authors wondering they'd identified something that could be applied to many post-infectious illnesses.

"Because of the highly varied characteristics of the pathogens studied here, these findings may plausibly be generalized to the host response to many infectious agents."

If they're right, some of the COVID-19 long haulers might have the same immune genetic predispositions that this study suggested people with ME/CFS do.

The Upshot

It's important to note that COVID-19 studies published thus far have not assessed long haulers – they're focused exclusively on what's happening early in the illness.

They are, however, starting to reach deep into what's happening in the early stages of COVID-19. We have never come close in ME/CFS to the kind of in-depth analysis of the immune response during an infection that we are beginning and will certainly continue seeing in COVID-19 patients. It's no wonder that people like Avindra Nath and Ron Davis are so eager to follow these patients. They are truly our chance to catch ME/CFS in the act.

While few long hauler studies have been published thus far, think how easy it would be so easy to turn these early COVID-19 studies into long hauler studies. All the researchers need to do would be to follow the progress of the patients in the study – and then look back and see if they can identify what was happening in people who turned out to be long haulers.

Several scenarios have been presented. All involve some period of strong immune activation

Poor early immune response leads to a massive cytokine storm later that damages the lungs and other organs and causes hospitalization. Researchers focused on hospitalised patients may, however, conclude that the fatigue, PEM, etc. that is present is the result of organ damage. Poor early immune response leads to a smaller cytokine storm later. The patient is able to fight off the virus while at home but has trouble recovering. Various hypotheses have been presented: the cytokine storm has triggered an autoimmune reaction (Nath), it has altered central nervous system functioning, or the virus has not been completely neutralized, or it has reactivated herpesviruses.

A strong early immune response causes a smaller but still potent cytokine storm. In the Dubbo hypothesis the patient is able to fight off the virus but the cytokine storm it triggered causes the microglia to go on to hyperalert – producing all the symptoms of ME/CFS, FM and others. We don't know if this strong early immune response actually occurred but it might have given that stronger symptoms were a risk factor for coming down with ME/CFS.

The Dicey Drug Issue

Thus far some studies and observations suggest that a poor early immune response in some COVID-19 patients may set up them up for a scorching immune response later (cytokine storm) that produces a dangerous positive inflammatory feedback loop. These patients appear to respond to immune suppressants. On the other hand, giving immune suppressants too early – or to people whose immune systems are fighting off the pathogen – is not beneficial.

Depending on where they are in their illness, people with COVID-19 could benefit from antivirals or immune suppressants. These drug studies are providing invaluable insights into the different ways the immune system responds to pathogens. If we can identify which immune mistakes have occurred in the long haulers, we will have likely come a long way.

It's clearly critical for us that long-haulers- particularly non-hospitalised long haulers – get into studies. "Cytokine storms", for instance, appear to play a major role in sending COVID-19 patients to the hospital – but we don't know if they're occurring in non-hospitalised patients. With many COVID-19 studies naturally focusing on hospitalised and more severely ill patients we need more data on non-hospitalised patients.

It's clear that studies embracing the immune system, genetics, the brain, autonomic nervous system, etc. are needed to study the long haulers. Dr. Nath's, Ron Davis's – if it can get the funding – and the Swedish ME/CFS Centre study will – and hopefully more will pop up.

Keeping the pretence going

Source: www.investinme.org//IIMER-Newslet-20-0701.shtml
July 2020

In the same week that Dr Anthony Fauci, Director of the USA National Institute of Allergy and Infectious Diseases and a member of the US government's Coronavirus Task Force, made this statement -

"...it's extraordinary how many people have a postviral syndrome that's very strikingly similar to myalgic encephalomyelitis/chronic fatigue syndrome."

then we saw NICE - The National Institute for Health and Care Excellence - issuing this bizarre statement -

> **NICE - Statement about graded exercise therapy in the context of COVID-19**
> NICE is aware of concerns about graded exercise therapy (GET) for people who are recovering from COVID-19. NICE's guideline on ME/CFS (CG53) was published in 2007, many years before the current pandemic and it should not be assumed that the recommendations apply to people with fatigue following COVID-19. The recommendations on graded exercise therapy in CG53 only apply to people with a diagnosis of ME/CFS as part of specialist care, and CG53 is clear that this should be part of an individualised, person-centred programme of care, with GET only recommended for people with mild to moderate symptoms.
>
> As the guideline is currently being updated, it is possible that these recommendations may change. The evidence for and against graded exercise therapy is one of the important issues the guideline committee is considering. NICE plans to consult on the updated guidance in November 2020.
>
> NHS England has recently published guidance on After-care needs of inpatients recovering from COVID-19 that includes advice on fatigue.
>
> July 2020

Apparently, the recommendations on graded exercise therapy in CG53 only apply to people with a diagnosis of ME/CFS. Nothing should surprise anyone about NICE and its behaviour toward ME. Their controversial guidelines were rejected by patients and (most) charities when finally published in 2007 (after being taken to a judicial review by ME patients).

They produced a derisory response to requests from patients and this charity to perform a full review of the guidelines in 2017. They only reluctantly agreed in 2018 to review the guidelines IiMER response. Then we witnessed their shambolic creation of a review committee [NICE guidelines develpment] - Turning a farce into a shambles. that was determined to create an unnecessary "balance" of viewpoints. It allowed participation in the committee by some after background lobbying - all away from the eye of the public and patients.

No surprise that this charity has no confidence in NICE or its present review committee.

Unwilling to sweep away the years of failure regarding ME they now bend credibility by advising against using graded exercise therapy (GET) for patients recovering from COVID-19 - while maintaining flawed guidelines for ME that retain this dangerous recommendation for ME patients. The hypocrisy of this situation provides a flimsy cover for ineptitude and the distortion of reality from NICE's latest statement from NICE would make even Donald Trump envious.

An establishment organisation that is supposed "improve outcomes for people using the NHS and other public health and social care services" instead distances itself from correcting previous flaws in its policies and guidelines by advising on one rule for COVID-19 patients and one, deleterious rule for ME patients.

They have been found out by patients and taken to court - yet still play gatekeepers for this engrained establishment bias that prohibits acknowledgement for the failures in their policies from past years.

While some are hoping that the COVID-19 pandemic might accelerate acceptance of ME and remove the stigma, misinformation and mistreatment of ME patients so NICE seem intent on continuing to make ME patients second class citizens - accepting the reality of COVID-19 but ignoring the long-standing grievances of ME patients. One might just call it discrimination.

It begs the questions - who is really controlling NICE policy? Who are they meant to be protecting?

In extensive correspondence with NICE director of guidelines Professor Mark Baker it became clearly evident that the NICE position on GET was untenable. The guidelines ought to benefit patients not the careers of some. Professor Baker admitted that the guidelines are unpopular with patients - even unfit for purpose.

Professor Baker stated that the existing guidance is carefully worded with nuances - and an implication that doctors are somehow not only aware of the nuances but are also understanding them. This ludicrous situation continues with the incomprehensible statement that COVID-19 patients should not have GET prescribed but that it is quite fine for ME patients to be the guinea pigs for the psychosocial lobby that still pervades UK healthcare.

We requested that NICE remove CBT and GET as recommendations for ME - immediately. NICE refused. We have stated it is illogical, and harmful to patients, that NICE retain the existing guidelines when it is admitted they are not fit for purpose, are not what patients want and will be discarded in any case. We have stated that there is no rational reason to maintain the existing guidelines if they do harm and that, at the very least, NICE must follow what USA have done and remove recommendations for using CBT and GET as treatments for ME with an addendum to the existing guidelines.

We have requested that this addendum is communicated to other healthcare agencies around the world who have misguidedly used the existing NICE guidelines as any basis for their own treatment of ME patients. NICE refused.

Professor Baker wrote to us that NICE “will discuss at the highest level at NICE what remedial action to help patients we can take in the meantime.” Nothing happened.

As we summarised in our earlier article NICE, and those deciding on the future for people with ME, must be held accountable if more people are harmed by retaining the existing damaging recommendations for using CBT and GET. NICE had a chance to help people with ME by using the logic of treatment of COVID-19 patients and revising immediately their recommendations of GET and CBT for ME. They failed again and instead issued another negligent statement.

The public rightly criticise government failings in handling COVID-19 - they must be held accountable. No such requirement seems to prevail for NICE.

Associated link that may be of interest…
https://www.meaction.net/2020/08/06/open-letter-demands-action-to-safeguard-people-with-me-not-just-post-covid-patients

Useful links for ME/CFS people during the Covid Pandemic

Source: www.actionforme.org.uk/news/useful-resources-following-yesterday%E2%80%99s-covid-19-restrictions

23rd September 2020

The following links/article have been taken from the Action for ME website

With yesterday's announcement about new UK restrictions relating to Covid-19, we know lots of you may be feeling concerned, let down and frustrated. While for many with M.E., lockdown is something you live with on a daily basis, the prospect of more pressure on the services and support you rely on is understandably worrying. Please know that we will continue to be here with information and support to help you cope, connect with others, and secure the services you need.

- Our Crisis, Advocacy and Support Service can share trusted information, support and signposting on accessing health and social care, welfare benefits and symptom management; and support you or your child with M.E. to advocate for your needs.

- Our free online forum for adults with M.E. offers peer-support and friendship with other people living with M.E.

- Our community for young people with M.E. (age up to and including 18) is free to join and offers a range of peer-support services, including pen pals, buddies for young people with severe M.E., and a safe, secure online forum.

- Our M.E. and Coronavirus page signposts to official government advice for people living in England, Northern Ireland, Scotland, or Wales.

- People with M.E. can use our 'This is M.E.' resource to help their carer or other support professional understand how M.E. impacts them, and the best ways to support them.

- Our shopping support resource, designed to share with supermarket staff, highlights that, as someone with a chronic neurological condition and at increased risk of severe illness from Coronavirus, you need access to priority shopping times.
- you could consider getting a sunflower lanyard which shows supermarkets you need extra support.

- The Shopping Slot website allows you to search for delivery slots for all the mainstream stores at once, using your postcode.

- Have you connected with your local Mutual Aid group or local Covid helpline (Google "Covid-19 helpline" + your area to see if there is one near you)?These volunteer-run services can help with shopping and other essentials.

If you're in need of support from our Crisis, Support, and Advocacy Service, you can contact them by calling 0117 927 9551 from 10am to 5pm Monday to Friday, or by emailing questions@actionforme.org.uk