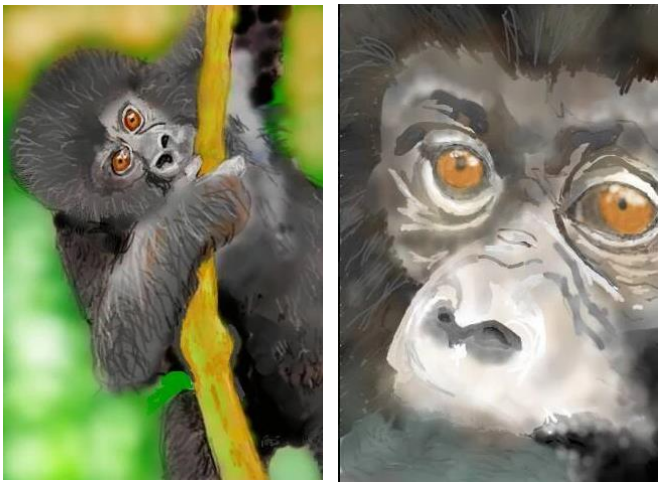
Guildford ME/CFS Support Group
(& West Surrey)

Newsletter

June 2019



#BEDFEST

As part of bedfest, the above art is by Soul in the Netherlands
www.bedfest.meaction.net

I got diagnosed twenty years ago then age 27. Being stuck to bed a lot of the time I developed a lot of new hobbies that I would be able to do from bed, singing in a virtual choir (they'll probably send in a recording), needlefelting, drawing, crochet, animation movies and keeping progress picture albums on Facebook of the things I make.

Future dates

Open to all members and carers

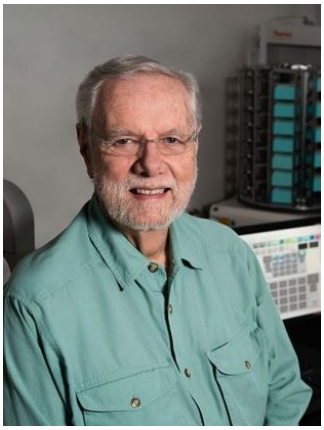
For details of meetings please email guildfordme@hotmail.co.uk

New blood-test biomarker for ME/CFS

Source: http://med.stanford.edu/news/all-news/2019/04/biomarker-for-chronic-fatigue-syndrome-identified.html?fbclid=IwAR2mHzFWNTAxcM9g3gnWoGIbU8JkKijUSiKbVQ7T1yyzDNyF9hjafp44c9E

29th April 2019

People suffering from a debilitating and often discounted disease known as chronic fatigue syndrome may soon have something they've been seeking for decades: scientific proof of their ailment. Researchers at the Stanford University School of Medicine have created a blood test that can flag the disease, which currently lacks a standard, reliable diagnostic test.



"Too often, this disease is categorized as imaginary," said Ron Davis, PhD, professor of biochemistry and of genetics. When individuals with chronic fatigue syndrome seek help from a doctor, they may undergo a series of tests that check liver, kidney and heart function, as well as blood and immune cell counts, Davis said. "All these different tests would normally guide the doctor toward one illness or another, but for chronic fatigue syndrome patients, the results all come back normal," he said.

The problem, he said, is that they're not looking deep enough. Now, Davis; Rahim Esfandyarpour, PhD, a former Stanford research associate; and their colleagues have devised a blood-based test that successfully identified participants in a study with chronic fatigue syndrome. The test, which is still in a pilot phase, is based on how a person's immune cells respond to stress. With blood samples from 40 people — 20 with chronic fatigue syndrome and 20 without — the test yielded precise results, accurately flagging all chronic fatigue syndrome patients and none of the healthy individuals.

The diagnostic platform could even help identify possible drugs to treat chronic fatigue syndrome. By exposing the participants' blood samples to drug candidates and rerunning the diagnostic test, the scientists could potentially see whether the drug improved the immune cells' response. Already, the team is using the platform to screen for potential drugs they hope can help people with chronic fatigue syndrome down the line.

A paper describing the research findings was published online April 29 in the Proceedings of the National Academy of Sciences. Davis is the senior author. Esfandyarpour, who is now on the faculty of the University of California-Irvine, is the lead author.

Providing the proof

The diagnosis of chronic fatigue syndrome, when it actually is diagnosed, is based on symptoms — exhaustion, sensitivity to light and unexplained pain, among other things — and it comes only after other disease possibilities have been eliminated. It is also known as myalgic encephalomyelitis and designated by the acronym ME/CFS. It's estimated that 2 million people in the United States have chronic fatigue syndrome, but that's a rough guess, Davis said, and it's likely much higher.

For Davis, the quest to find scientific evidence of the malady is personal. It comes from a desire to help his son, who has suffered from ME/CFS for about a decade. In fact, it was a biological clue that Davis first spotted in his son that led him and Esfandyarpour to develop the new diagnostic tool.

The approach, of which Esfandyarpour led the development, employs a "nanoelectronic assay," which is a test that measures changes in miniscule amounts of energy as a proxy for the health of immune cells and blood plasma. The diagnostic technology contains thousands of electrodes that create an electrical current, as well as chambers to hold simplified blood samples composed of immune cells and plasma.

Inside the chambers, the immune cells and plasma interfere with the current, changing its flow from one end to another. The change in electrical activity is directly correlated with the health of the sample.

The idea is to stress the samples from both healthy and ill patients using salt, and then compare how each sample affects the flow of the electrical current. Changes in the current indicate changes in the cell: the bigger the change in current, the bigger the change on a cellular level. A big change is not a good thing; it's a sign that the cells and plasma are flailing under stress and incapable of processing it properly. All of the blood samples from ME/CFS patients created a clear spike in the test, whereas those from healthy controls returned data that was on a relatively even keel.

"We don't know exactly why the cells and plasma are acting this way, or even what they're doing," Davis said. "But there is scientific evidence that this disease is not a fabrication of a patient's mind. We clearly see a difference in the way healthy and chronic fatigue syndrome immune cells process stress." Now, Esfandyarpour and Davis are expanding their work to confirm the findings in a larger cohort of participants.

Doubling up
In addition to diagnosing ME/CFS, the researchers are also harnessing the platform to screen for drug-based treatments, since currently the options are slim. "Using the nanoelectronics assay, we can add controlled doses of many different potentially therapeutic drugs to the patient's blood samples and run the diagnostic test again," Esfandyarpour said.

If the blood samples taken from those with ME/CFS still respond poorly to stress and generate a spike in electrical current, then the drug likely didn't work. If, however, a drug seems to mitigate the jump in electrical activity, that could mean it is helping the immune cells and plasma better process stress. So far, the team has already found a candidate drug that seems to restore healthy function to immune cells and plasma when tested in the assay. The drug, while successful in the assay, is not currently being used in people with ME/CFS, but Davis and Esfandyarpour are hopeful that they can test their finding in a clinical trial in the future.

All of the drugs being tested are either already approved by the Food and Drug Administration or will soon be broadly accessible to the public, which is key to fast access and dissemination should any of these compounds pan out.

Davis is a member of Stanford Bio-X, the Stanford Cancer Institute and the Stanford Maternal & Child Health Research Institute.

Other Stanford authors of the study are research scientists Mohsen Nemat-Gorgani and Julie Wilhelmy and research assistant, Alex Kashi.

The study was funded by the Open Medicine Foundation. Davis is the director of the foundation's scientific advisory board.

Stanford's departments of Genetics and of Biochemistry also supported the work.

MEpedia

Source: https://me-pedia.org/wiki/Welcome_to_MEpedia

MEpedia is a project founded by MEAction, powered by the patient community, and built by volunteers including patients, students, and researchers. We are crowd-sourcing a knowledge base on the history, science and medicine of ME, CFS, and related diseases. Jump in!

"Great misery has been inflicted unnecessarily" says UN reporter

Source: www.actionforme.org.uk/news/great-misery-has-been-inflicted-unnecessarily-says-un-reporter

23rd May 2019

“Great misery has been inflicted unnecessarily, especially on the working poor, on single mothers struggling against mighty odds, on people with disabilities who are already marginalized,” says UN reporter Prof Alston.

Yesterday, the UN Rapporteur on extreme poverty and human rights in the UK, Philip Alston, released his final report summarising his findings from his tour of the UK.

As part of the UN’s commissioned report, Alston spent two weeks visiting cities in England, Wales, Scotland and Northern Ireland and speaking with people living in poverty. The report found that Britain was in breach of four UN human rights agreements relating to disabled people, women, children and economic and social rights. When discussing the impact that austerity has had on society, Alston accuses the government of creating a society where the UK’s welfare safety net has been “deliberately removed and replaced with a harsh and uncaring ethos”, which has caused “tragic social consequences.”

Amongst issues that the UN Rapporteur highlighted within the report, the impact that the Government’s policy of austerity and welfare benefit policies has had on those with disabilities and their families is severe. Nearly half of those impoverished, 6.9 million people, are from families including a disabled person. Alongside this, disabled people are more likely to be unemployed, in insecure employment, or economically inactive.

Although Alston cannot deny that some good outcomes achieved in the overturning of Britain’s “post-war Beveridge social contract”, these outcomes have not been able to stop the decline in economic stability for the least well off. The shocking rise in homelessness, food-banks, “decimation of legal aid”, falling life expectancy for some, denial of benefits to severely disabled people, as well as much more are evidence to this.

Alston criticises welfare policies that deliberately “built a digital barrier that effectively obstructs many individuals’ and creates “delay tactics” through processes such as mandatory considerations. Preliminary results from our Big Survey which is open until Friday 2 August, show that one in four people with M.E. have found the process for applying for Universal Credit difficult because they don’t have access to the internet or are unable to use a computer due to the impact it has on their condition.

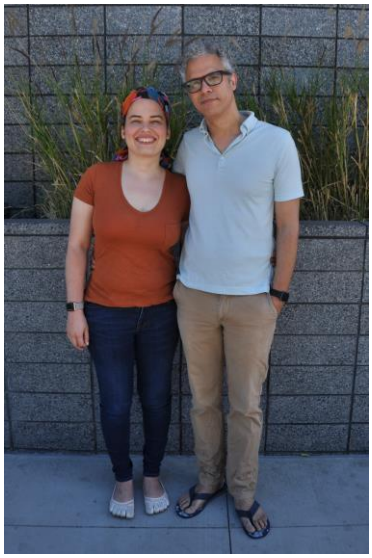
Jennifer Brea in remission

Source: https://medium.com/@jenbrea/health-update-3-my-me-is-in-remission-dd575e650f71

Heartfelt congratulations to Jennifer Brea for her recent huge health improvement

Jennifer Brea: health activist, filmmaker, Unrest director, #MEAction co-founder, TED Talker.

This is a hard post to write because there are no words that can do this justice. I can hardly believe it myself. My ME is in remission.



For the first few years that I was ill, I dreamt of being able to say this. I fantasized about what recovery would be like. And then, I can't remember when, I stopped dreaming. It wasn't that I gave up hope. Rather, I knew I had to move on from something that might never happen and learn how to live the life that I had. And now, thanks to three spinal surgeries—one for something called craniocervical instability and the others for tethered cord syndrome—I believe I am on my way to a full recovery.

If you are just stumbling across my story or the journey I've been on the last 12 months, which started after surgery for thyroid cancer, please read, "A new diagnosis to add to the list" and if able, all the posts in the "CCI+Tethered Cord" series. (ME stands for myalgic encephalomyelitis, commonly called "chronic fatigue syndrome.")

I remember when the rustling of my own sheets from the slightest movement, a sound imperceptible to the normal human brain, would cause indescribable, searing pain. Now, I can go to a cafe and sit next to a couple having a conversation, music with lyrics playing over the steady din of the other diners, while typing this post on my computer and I am totally fine.

I've spent the last eight years mostly in my bedroom. At my worst, I lived in bed, able only to walk to the bathroom a couple of times a day. At my best, I could leave my house in a power wheelchair. Even then, I had to be careful about pacing out how much I did and when. Now? I haven't used my wheelchair in seven weeks. If I feel like having chocolate, I'll walk two blocks to the grocery store and get it. I can get into a Lyft without my wheelchair and know I'll be able to navigate whatever distances or obstacles I might face on the other side. Most of what I want to do I can do, and never crash.

Now, I walk for exercise. I walk for the sheer thrill of it. I reach a speed where my feet start rising from the ground until I'm about to launch into a sprint. I feel like I have the energy to just go flying down the street (if not the body—I'm not supposed to do high-impact activities for a year post-fusion and it may never be a good idea).

I used to be allergic to sunlight and now I'm not. I used to feel ill if I stood still for even a minute or two, and now I can stand seemingly forever. Now, when I sit in a chair, it's with my feet planted on the ground.

Last year, I once tried to go into a pool and although I didn't even move, just the act of being in slightly cool water overwhelmed my ability to regulate my body temperature and I crashed—hard. Last week, I did an hour of water aerobics. Picking up a heavy dinner plate used to provoke neurological symptoms. Now, several times a week, I lift light weights, for 30–90 minutes. And if I want to, I can do it again the next day.
This week, when my husband came to pick me up from the airport in Philadelphia, he walked passed me three times. He didn't recognize me. He was looking for a woman sitting on the ground.

By any definition, I no longer meet the criteria for myalgic encephalomyelitis. My physical and cognitive post-exertional malaise (PEM) are both gone. I have not crashed since I left the hospital. My POTS is gone. My peripheral neurological symptoms, sound sensitivity, sensory processing challenges, difficulty regulating my body temperature, intracranial pressure, brain inflammation and muscle fatigability are all gone. I am off Valcyte, Famvir, Mestinon, and all other ME or POTS drugs.

It is now clear that all of my symptoms had a mechanical mechanism: brainstem compression (likely with altered cerebrospinal fluid and cranial blood flow) due to cranial settling and craniocervical instability (CCI), in combination with tethered cord syndrome.

Given my remarkable improvements, the centrality of those structural mechanisms is, in my case, undeniable. What remains elusive is the root cause. I know that CCI caused my PEM and other ME symptoms. I can never know why I developed CCI in the first place. (I do have some conjectures!) And I have good reason to think that so long as my fusion holds and my spinal cord does not re-tether, my PEM and other symptoms will never come back.

It is worth emphasizing that a year ago today, if you told me all this would happen, that this could be my outcome, I would not have believed you. I was an acute, post-viral onset patient. I have never had any symptoms that I would have interpreted as structural, rather than systemic. I never had any discernible problems with my neck. As it turned out, the mechanism was structural. Its impacts were systemic.

That's not to say I don't still have some challenges. It takes time to recover from these surgeries. After eight months in a cervical collar, I had to build up my neck muscles until they were strong enough to hold the weight of my head throughout the day. Because of my back surgery, it can still be difficult for me to sit in a chair for too long (standing is easier). I still sometimes have stiffness, swelling or pain in my neck or vague, but generally transient, neurological symptoms. All of this is getting milder and less frequent with time, physical therapy, and strength training. I am also deconditioned. I still don't have the endurance of an average person. For seven years, I was mostly in beds and wheelchairs, and was completely flat and on a catheter (not even transitioning to a commode) for a good part of my eight week hospital stay. It's going to take time to recondition both my muscles and my peripheral nervous system. When I exert myself, I do get fatigued, and will often drop hard by the end of the day, but it's an entirely different thing from when I had ME.

Before my surgery, I would never have been able to exercise. Any activity beyond my extremely circumscribed limits would make me feel worse, perhaps permanently, causing a "crash" of my autonomic, central and peripheral nervous systems. Now, for the first time in eight years, I can feel the healthy fatigue of a day well spent. Every day, I try to push myself a little harder. The next day, I wake up sore and stiff, like I've just run a marathon. I can feel the lactic acid in my muscles, and sometimes my brain. At the beginning, I'd wonder if my PEM had come back, but then if I got up and started moving, the pain, stiffness and lactic acid would dissipate. Whereas before my surgeries, movement always made me worse, now it actually helps me feel better. The more physical activity I do, the stronger I get. Up is up again.

I do still have mast cell activation syndrome for which I take Ketotifen, but even that seems like it is improving and may eventually go away. In the last many weeks, I seem to be becoming less and less reactive to mold and my other mast cell triggers.

The other reason why this post is hard to write is I don't feel about this miracle at all the way I thought I would. Part of it is that recovery is a process. While I found immediate benefit from the surgeries, it wasn't like I woke up, the skies parted, and suddenly I was an average human again. My surgeon told me 50% of my outcome had just happened in his operating room and 50% would be the work I put in over the next twelve months, and every week I learn why that is truer than I could have known. I also feel like I've just come back from a war, and it's left scars I didn't know were there. This experience has changed me forever, in good ways and in hard ways. Now that I finally have the space and health to truly feel what any normal human might feel about the last eight years, I sometimes wish I didn't. The grief and trauma over what this illness has destroyed has come rushing in, for me and for Omar; the meaning of the time that we will never get back. We are so lucky to have this new chance, and we know there are so many who have had to live through much worse for far longer, but we just don't feel lucky yet. My husband slept on an airbed in a hospital room for nearly three months, through many nights of me waking up in excruciating pain, all while trying to keep working and keep our world together. Right now, we just feel exhausted.

I also can't help but look at everything that's happened to me and feel even angrier about the conversion disorder diagnosis I received in 2012 (made on the basis of my tethered cord symptoms). Angry how unlikely it was in this medical system that, even if I had lived another fifty years, I would ever have found out what was causing my symptoms.

I also can't help but feel something approaching survivor's guilt. Why did I get this lucky? How do we make sure everyone who needs these surgeries has the choice to have them? How can we uncover all the causes and all the cures for all the mechanisms that might underlie different patients' ME?

On that point, I want my story to be a source of hope. I did not get better by thinking positively or drinking green juice (even though I'm sure both are good for almost everybody). I found the specific cause of my symptoms, backed by both subjective and objective measurement. I then had three fairly long and complex neurosurgeries to address this cause, and am now on a path to recovery.

This was possible because surgeons have been doing craniocervical fusions on patients for more than fifty years. At first, the surgery was for patients who had had acute traumatic accidents. Later, it was used for craniocervical instability due to tuberculosis, to people born with congenital risk factors for developing CCI, like Little People and people with Downs Syndrome, and craniocervical instability due to inflammatory conditions like Rheumatoid Arthritis.
More recently, craniocervical fusion surgeries are being used to treat patients with craniocervical instability due to genetic connective tissue disorders, especially hypermobile Ehlers-Danlos Syndrome. And now, Jeff Wood and I are the first two patients (as far as we know) to meet the International Consensus Criteria for ME and to have our ME resolve due to this fusion surgery. (At least 20 patients with ICC-ME who are part of the online community have been diagnosed with CCI in the last year.)

Measurements, techniques, and treatments developed in one scientific or medical context can often be applied to people living with other diseases. While for decades, people with ME have been frozen in amber due to gross neglect from the medical community and government agencies, all around us, science and medicine have continued to advance. While that should be a source of pain and anger, it should also be a source of hope. Whatever the cause or central mechanism of your ME, there is a reasonable chance that when it is discovered, a treatment may already exist, waiting to be applied to a population it never imagined could need it. That discovery could come from a clinician or researcher. It could also come from an unusually dogged and creative patient, like Jeff, like you.

Whatever those treatments turn out to be, I know we will have to fight for them. Fight to scientifically validate them. Fight to educate doctors about them. Fight to ensure that everyone, no matter their country, health system, or financial means, has access to diagnosis and effective care. I still have a long way to go in my recovery but no matter how well I get, I will never stop fighting for that future.

I have so much more to say, and will in future posts, about why I think I developed craniocervical instability (CCI), how CCI might cause post-exertional malaise (and other dysautonomias), how the totally fascinating way I was diagnosed raises important questions about this disease, the process of surgery, of recovery and the way forward. I also want to talk about privilege and access. I want to do all these things…for now, though, a moment to reflect, to heal, to give thanks and to gear up for the fight ahead.

To learn more, follow me on Medium and see the full series of posts on CCI and Tethered Cord Syndrome. Also check out Jeff's website, which talks more about diagnosis. You can also "Ask Me Anything" on this Reddit Ask Me Anything post or by tweeting to me @jenbrea.

Rare gene mutations may be affecting energy levels in ME/CFS

Source: www.prohealth.com/me-cfs/library/rare-gene-mutations-may-affecting-energy-levels-cfs-91300

By Cort Johnson 15th June 2019

Dr. Camille Birch has a PhD in biomedical engineering and hails from the Hudson Alpha Institute for Biotechnology at Huntsville, Alabama. Hudson Alpha, only 11 years old, is one of those new biotechnology efforts that's using sophisticated bioinformatics to understand how our genes affect our health.

Dr. Liz Worthey and Dr. Birch believed that genetic mutations in ME/CFS might be altering metabolic pathways and causing an "unstable cellular energy state" in ME/CFS. They're using a variety of algorithms, including one called "custom network analysis", to examine all sorts of genomic abnormalities (single nucleotide substitutions, structural variants, fusion products, expanded tandem repeats, and variants in regulatory regions). (Yes, our genome is very complex…)

The type of ME/CFS you have, they think, might depend on which metabolic pathways your genetic mutations are whacking. Boy, does it appear that they hit that nail on the head in this study.

Genetic diseases

Dr. Birch pointed out that mutations in just one gene can cause a bogglingly wide variety of illnesses. Mutations in just one gene called lamin-A, for instance, are associated with no less that 11 diseases – many of which have no relationship to each other!

On the other end of the spectrum, all 14 subtypes of glycogen storage disease are associated with completely different genes. These genes affect glycogen synthesis, breakdown or in other ways, but all of them end up impacting energy production.

One gene and its genetically modified protein, then, could conceivably be responsible for all the different manifestations of ME/CFS, or, on the other end of the scale, a raft of mutations in different genes could be responsible for, or contribute to, what we know of as ME/CFS.
This study looked at ten patients from Dr. Younger's cohorts, but what it lacked in size it appeared to make up in depth.

Risky Loci

First they looked at relatively common gene variants or mutations found in the general population and known to have negative effects. They have found 32 of what they called "risk loci" in ME/CFS.

It wasn't the individual risk loci which stood out, though: it was the pattern present in them. Geneticists always like it when closely aligned genes pop up in their studies. That suggests a problem – perhaps large enough to cause disease – is showing up in one area of the body. Birch's sample size was small, and she needed a way to zero in on the potentially relevant genes. When she asked the program if, say, 30% of the general population has a certain variant, what was the probability that a large portion of her ME/CFS group had that variant?

The program told her that it was extremely unlikely that 5 of the 32 loci would be found at such high levels in the ME/CFS group. Bigger studies are clearly needed, but given the probability that these were real findings – that these gene mutations likely are present and possibly doing some damage in ME/CFS – she turned to those.

Three of the five, remarkably, were associated with one part of the immune system – the interleukins (IL-1, IL-12B, IL-4R). Another affects cellular energy production, and the last affects nitric oxide production – which is important in blood vessel functioning (vasodilation) and inflammation. The fact that all five – impacting energy, the immune system and possibly blood vessel functioning – fit this disease well was definitely encouraging.

Rare or unique variants
It got better, though, when the group searched for rare or unique gene mutations found in the ME/CFS group. Each person had an average of 14 rare or unique gene mutations. The good news is that the rare mutations, while quite variable, also made sense – hitting metabolic, immune, ion and mitochondrial pathways.

In keeping with the results of past studies, no rare mitochondrial gene variants were found. As we'll see, though, it's not necessary to take a two-by-four to the mitochondria to whack someone's energy production – there are plenty of subtler ways to do that.

The fact that most of the rare gene mutations were unique to each patient presented problems. Determining which ones might be causing ME/CFS required an unusual kind of digging. It was time for Birch to get personal.

After taking notes on 60 of the 120 stories of ME/CFS presented on the Solve ME/CFS Initiative's website, she realized that ME/CFS was more heterogeneous than she'd known. A variety of potential subsets jumped out at her – each of which could have a different molecular basis.

- About 1/3rd described an infectious type onset.
- About 10% never felt normal, but the problem didn't get bad until they hit their teen to adult years. This group slowly got worse over time.
- Another small group described an extremely rapid and massive onset triggered by a non-infectious event – surgery, trauma or other very stressful event.
- A few people described cognitive problems so severe that they sounded like they had something like Parkinson's.
- Another group described really severe pain.
- Another group had really severe orthostatic intolerance.

She needed some more information, though, and asked each person an additional 32 questions (!) that would help the researchers guide their analysis. She's basically doing a precision genetic analysis – examining each person's story in detail – and using that information to better understand their genetic results. Included were some open-ended questions which allowed the participants to just tell it like it is in their own rich detail.

She's now analysing that data, but even without it the preliminary genetic analysis provided some intriguing possibilities. Every one of those ten patients had genetic issues in three pretty darn exciting categories.

Energy metabolism
The first was energy metabolism, a subject that's getting more and more attention all the time. Another nice pattern formed when she found that three of the patients had a potentially very damaging and rare gene mutation that affected the AMPK energy sensing pathway – which studies have suggested may be compromised in both ME/CFS and fibromyalgia.

None of the genes have been associated with a disease before – which, in my book, counts as a plus. Intriguingly, these genes are closely related – one tells AMPK to ramp up, another to ramp down, and another has an intermediate role. That close relationship suggests that different kinds of damage to AMPK could result in the same kind of fatiguing problems.

AMPK ensures that proper ATP levels are present in our cells. As ATP declines during exercise, for instance, AMPK ensures that more ATP is produced.

Way back in 2003, Dr. Grahame Hardie ("Management of cellular energy by AMPK") suggested that AMPK problems were present in ME/CFS at a MERUK Workshop talk. AMPK should get activated in our muscle cells during exercise, but more recently, when Julia Newton in the U.K. whacked the muscle cells from ME/CFS patients with exercise, AMPK didn't respond…
In type II diabetes, AMPK activation issues produce "metabolically inflexible" muscles that have trouble switching between glucose and fatty acid metabolism. Researchers refer to the reduced skeletal muscle mitochondrial capacity that results as "mitochondrial overload".
Interestingly, if AMPK is a problem, a wide variety of treatments may be able to help.

Iron metabolism
They found rare and damaging mutations in two people with ME/CFS in iron-metabolizing genes that could cause trouble transferring iron from the liver or in iron recovery. Because iron carries oxygen to our cells – which then use the oxygen to produce energy – it's no surprise that iron deficiency diseases such as anemia can cause enormous fatigue.

If an anemia is present in ME/CFS, though, it's a very different kind of anemia than what we're used to. Birch brought up the interesting possibility that if anemia is present in ME/CFS – it's not present in the blood – it's present in the tissues.

That was an interesting possibility. Throw in another admittedly very preliminary (and not genetic) report from an ongoing study at Ian Lipkin's research centre – and the iron issue gets even more interesting. Instead of examining the makeup of the genes we are born with, Lipkin is examining which genes are active.

In a possible tie-in, Lipkin found that several genes associated with iron metabolism were less active in ME/CFS patients. The differences were modest, but because they showed up in one pathway (that pattern thing again), Lipkin thought the ultimate impact could be significant.
In fact, Lipkin stated that, based on their "very early" data, they could predict that lesions in four parts of the iron intake pathway into the cell could be present. Not getting iron (and oxygen) into the cell could, of course, put quite a damper on energy production and wreak havoc with the resulting oxidative stress. Problems with that pathway could spell trouble in two potentially very important aspects of ME/CFS: oxidative phosphorylation (ATP production) and oxidative stress.

Glycogen storage disease?
So far, Birch had found rare and damaging mutations that could very well impact energy production in five out of ten patients in that study. Would the trend continue? Would we be so lucky? Rather remarkably, we were. In fact, Birch actually saved the best for last. In what she described as another surprise, mutations in glycogen storage genes showed up in two people. Both mutations are very, very rarely found in the general population. One gene codes for an enzyme called enolase 3, which is associated with a glycogen storage disease (GSD 13) which, interestingly enough, shows up in adults (check), is characterized by severe muscle pain post exercise (PEM; check), and is associated with an intolerance of exercise (double check!). It's one of two GSD's associated with "exercise intolerance".

Birch was very calm, but I was about jumping out of my seat when she described a genetic disease with adult onset, severe muscle pain after exercise, and exercise intolerance.
The plot thickened further when she reported that GSD 13 is thought to be very (VERY) rare – as in present in only two families thus far. She noted that that fact is almost irrelevant, because, if no one is testing for this disease (it requires a muscle biopsy) – and few doctors probably are – it's going to be rare no matter how many people are affected. It's not uncommon at all to later find that "rare diseases" aren't so rare after all.

If the mutation causes severe muscle pain after exercise and exercise intolerance, one wonders how many people with FM or ME/CFS may have been misdiagnosed? Will GSD 13 be like craniocervical instability – a rare condition or disease with a difficult diagnosis – which doctors just haven't been testing for?

Of all the GSD's, GSD 13 is clearly potentially the most relevant for ME/CFS. Most of the other GSD's produce in young children low blood glucose levels, enlarged livers, swollen bellies, heat intolerance, slowed growth and muscle cramping/pain after exercise.

GSD 13 – which is not even mentioned in some medical websites, including the Association for Glycogen Storage Diseases (lol) and the Cleveland Clinic (but is in Wikipedia – go figure) – does not cause hypoglycemia, enlarged livers, swollen bellies, etc., but is one of only two GSD's that causes "exercise intolerance" and "an increasing intensity of muscle pain over the decades" (check!).

It "appears" to be extremely rare. The website on which the most GSD 13 information is found states under epidemiology – 3 patients (!). The clinical pool is obviously very small, but the website states that muscle strength is usually normal, episodic elevations of serum creatinine kinase can occur, which are reduced and can be normal with rest, and that episodic rhabdomyolysis may occur. (Rhabdomyolysis is a serious event which occurs when muscle fibres rapidly break down and release so much muscle detritus into the blood that kidney failure can result.) Beyond that, it appears that we know little about the disease.

Lastly, another patient had a mutation in another gene associated with a glycogen enzyme (glucosidase alpha neutral C) that could impact glycogen storage, but not much is known about that enzyme or gene. I don't know if I particularly want the answer to be a rare genetic disease (lol) but I certainly want answers. Whether or not GSD 13 is present in ME/CFS, the potential glycogen storage issue, as well as the AMPK and iron issues appear to open up more possibilities.

Conclusion

It's important to note that Birch is not hunting for rare AMPK or ion metabolism or glycogen metabolism gene mutations – they are simply the ones that are popping up. They popped up in 7 of the 10 patients.

So far, ME/CFS is looking more like a glycogen storage type disease than anything else: rare, different gene mutations have popped up that could produce problems with energy production in different ways. Of course, we don't know if these gene mutations are having an effect or if they're present in other ME/CFS patients. The body is complex with many redundancies. Just because you have a rare and potentially damaging gene mutation doesn't mean it's impacting your health, and, indeed, Dr. Birch warned that the study is quite small and that as more patients are added and they dig deeper molecularly, some of these avenues may not pan out.

Dr. Birch emphasized their desire to collaborate with others and stated they were actively talking to other ME/CFS researchers as well as geneticists outside the ME/CFS world – and then mentioned two. She said she spoke to Nancy Klimas at the last NIH conference and to a UK researcher involved in a very large genetic study.

That's just the tip of the iceberg in this evolving field. Avindra Nath at the NIH should certainly know about this research – he's doing muscle biopsies – possibly right now – and genetics work; Ron Tompkins of the Open Medicine Foundation's Collaborative ME/CFS Research Centre at Harvard will be doing the deepest dig in ME/CFS patient's muscles yet; Ian Lipkin would probably love to hear of more evidence of iron metabolism issues; Allan Light in Utah has been involved in several genetic studies and a family study is underway at the Bateman Horne Centre. Of course, there's Ron Davis at Stanford – our in-house genetics expert – who is overseeing a personalized approach to the genome in studies of families with ME/CFS, as well as other genetic studies with the Open Medicine Foundation's help.

When contacted, Ron Tompkins said his team would be assessing glycogen issues in the muscle biopsies they're doing. The group's findings were presented at a clinical genetics conference recently and were "received really well". The presenter said the frustrated doctors (they are frustrated, too) were quite eager to get some potential answers for this disease.

Liposomal vitamin C

Although the exact cause of ME/CFS is unknown it is often associated with a viral trigger and a lot of research indicates a resulting autoimmune condition. Epstein-Barr virus (AKA the autoimmune virus) is a common subject in ME/CFS circles. Viruses are so small that once we encounter any virus copies of it are destined to roam around our bodies forever, sometimes reactivating (by blundering into just the right part of us) and requiring our immune system to keep them in check. An on-going low level reactivation of a virus such as EBV might be a factor for some?

Our newsletter aims to be informative not prescriptive and any supplements or treatments mentioned in our newsletters are tried at your own risk. That said, high-dose or liposomal vitamin C might be worth exploring. Medical conditions such as Hemochromatosis (inability to control iron levels) should be ruled out because Vitamin C enhances absorption of Iron.

The following 2 articles offer some insight about Vitamin C. The first more general, the second focused on EBV and antiviral benefit of Vitamin C. These are then followed by examples of high dose vitamin C supplement and liposomal vitamin C supplement.

Newsletter Editor

Article 1 – WebMD, Vitamin C

Source: www.webmd.com/diet/features/the-benefits-of-vitamin-c#1

Vitamin C is one of the safest and most effective nutrients, experts say. It may not be the cure for the common cold (though it's thought to help prevent more serious complications). But the benefits of vitamin C may include protection against immune system deficiencies, cardiovascular disease, prenatal health problems, eye disease, and even skin wrinkling.

A recent study published in Seminars in Preventive and Alternative Medicine that looked at over 100 studies over 10 years revealed a growing list of benefits of vitamin C.

"Vitamin C has received a great deal of attention, and with good reason. Higher blood levels of vitamin C may be the ideal nutrition marker for overall health," says study researcher Mark Moyad, MD, MPH, of the University of Michigan. "The more we study vitamin C, the better our understanding of how diverse it is in protecting our health, from cardiovascular, cancer, stroke, eye health [and] immunity to living longer."
"But," Moyad notes, "the ideal dosage may be higher than the recommended dietary allowance."

How much Vitamin C Is enough?

Most of the studies Moyad and his colleagues examined used 500 daily milligrams of vitamin C to achieve health results. That's much higher than the RDA of 75-90 milligrams a day for adults. So unless you can eat plenty of fruits and vegetables, you may need to take a dietary supplement of vitamin C to gain all the benefits, Moyad says. He suggests taking 500 milligrams a day, in addition to eating five servings of fruits and vegetables.

"It is just not practical for most people to consume the required servings of fruits and vegetables needed on a consistent basis, whereas taking a once-daily supplement is safe, effective, and easy to do," Moyad says. He also notes that only 10% to 20% of adults get the recommended nine servings of fruits and vegetables daily.

Moyad says there is no real downside to taking a 500-milligram supplement, except that some types may irritate the stomach. That's why he recommends taking a non-acidic, buffered form of the vitamin. "The safe upper limit for vitamin C is 2,000 milligrams a day, and there is a great track record with strong evidence that taking 500 milligrams daily is safe," he says.

Vitamin C, also known as ascorbic acid, is necessary for the growth, development and repair of all body tissues. It's involved in many body functions, including formation of collagen, absorption of iron, the immune system, wound healing, and the maintenance of cartilage, bones, and teeth.

Vitamin C is one of many antioxidants that can protect against damage caused by harmful molecules called free radicals, as well as toxic chemicals and pollutants like cigarette smoke. Free radicals can build up and contribute to the development of health conditions such as cancer, heart disease, and arthritis.

Vitamin C is not stored in the body (excess amounts are excreted), so overdose is not a concern. But it's still important not to exceed the safe upper limit of 2,000 milligrams a day to avoid stomach upset and diarrhea.

Water-soluble vitamins must be continuously supplied in the diet to maintain healthy levels. Eat vitamin-C-rich fruits and vegetables raw, or cook them with minimal water so you don't lose some of the water-soluble vitamin in the cooking water.

Vitamin C is easily absorbed both in food and in pill form, and it can enhance the absorption of iron when the two are eaten together.

Deficiency of vitamin C is relatively rare, and primarily seen in malnourished adults. In extreme cases, it can lead to scurvy -- characterized by weakness, anemia, bruising, bleeding, and loose teeth.

Article 2 – Effect of high dose Vitamin C on Epstein-Barr viral infection

Source: https://riordanclinic.org/research-study/effect-high-dose-vitamin-c-epstein-barr-viral-infection

The Epstein-Barr virus (EBV) is a member of the herpes family that targets lymphocytes and epithelial cells. It binds to B-lymphocytes via the CD21 cell surface protein, and establishes life-long persistence in memory B-cells. While the infection is usually benign, it can in some cases lead to acute infectious mononucleosis and can impair the immune system. EBV is linked to several malignancies, including Burkett's lymphoma, post-transplant lymph-proliferative disease, Hodgkin's disease, and several autoimmune diseases.

There is currently no treatment for removing EBV infections. Our clinic has been long interested in the use of vitamin C (ascorbic acid, ascorbate) to combat viral infections. Ascorbic acid is an essential nutrient that functions as a key water soluble antioxidant and is involved in synthesis of collagen, carnitine, and neurotransmitters. It affects wound healing, energy metabolism, nervous system function, and immune cell health. Oral supplementation with vitamin C typically gives rise to plasma ascorbate concentrations less than 0.2 mM, while high dose intravenous infusion of the vitamin can raise plasma concentrations higher than 14 mM. These "pharmacologic" plasma ascorbate concentrations, achieved by intravenous infusion have been linked with benefits to endothelial function, cellular immune function, antioxidative capacity, pain relief, and treatment of cancer and other illnesses.

The motivation for using intravenous infusions of Vitamin C (IVC) to treat viral illnesses comes, in part, from observations that virally infected patients exhibit vitamin C deficiency. This in turn suggests that clinical management of viral infections may benefit from supplementation. Improved recovery of subjects with viral infection upon supplementation with pharmacologic doses of vitamin C has been observed clinically. In a multicentre cohort study, sixty-seven symptomatic Herpes-Zoster patients were given intravenous vitamin C in addition to standard treatment for shingles. Pain assessments were made and dermatologic symptoms such as haemorrhagic lesions were followed during twelve weeks of treatment. Pain scores and number of dermatomes all showed statistically significant decreases during the treatment.

Several mechanisms of action have been proposed for this potential benefit.

- Since viral infections are often associated with oxidative stress, the ability of ascorbate replenishment to promote a reducing environment could be important in detoxification and neutralization of reactive oxygen species associated with infection.
- Vitamin C is also necessary for neutrophil function, as they typically accumulate ascorbic acid at 80 times the plasma concentration.
- Also considered as potential mechanisms are the ability of ascorbic acid to stimulate the production of interferon and other anti-viral cytokines, its ability to down regulate inflammation, and its direct antiviral properties.

Our study details an analysis of EBV progression, via antibody assays, in patients undergoing intravenous vitamin C therapy. The data were obtained from the patient history database at the Riordan Clinic. Among people in our database who were treated with intravenous vitamin C (7.5 g to 50 g infusions) between 1997 and 2006, 178 patients showed elevated levels of EBV EA IgG (range 25 to 211 AU) and 40 showed elevated levels of EBV VCA IgM (range 25 to 140 AU). Most of these patients had a diagnosis of chronic fatigue syndrome, with the rest being diagnosed as having mononucleosis, fatigue, or EBV infection. Our results, detailed below, add further evidence to the idea that ascorbic acid may be useful in treating viral infections.

Our analysis suggests the following:

- High dose intravenous vitamin C therapy has a positive effect on disease duration and reduction of viral antibody levels.
- Plasma levels of ascorbic acid and vitamin D correlated with levels of antibodies to EBV.
- There is an inverse correlation between EBV VCA IgM and vitamin C in plasma in patients with mononucleosis and CFS meaning that patients with high levels of vitamin C tended to have lower levels of antigens in the acute state of disease.
- The relation was found between vitamin D levels and EBV EA IgG with lower levels of EBV early antigen IgG for higher levels of vitamin D.
- Our clinical study of ascorbic acid and EBV infection showed the reduction in EBV EA IgG and EBV VCA IgM antibody levels over time during IVC therapy that is consistent with observations from the literature that millimolar levels of ascorbate hinder viral infection and replication in vitro.
- We published our results in a peer-reviewed journal: Effect of high dose vitamin C on Epstein-Barr viral infection. Mikirova N, Hunninghake R. Medical Science Monitor, 2014; 20:725-732

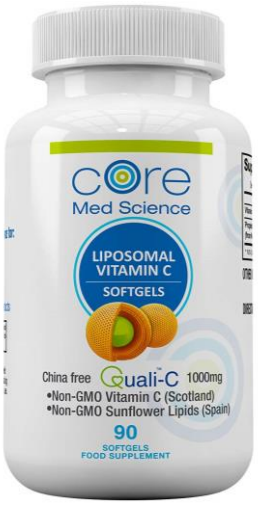
Typical Vitamin C supplement type

The article above refers to intravenous Vitamin C which is not casually available. Whilst not achieving intravenous levels, the following typical Vitamin C supplement is the most economical form. Liposomal is a means of hiding a supplements inside a package of fatty acids that are absorbed by the digestive system and the cells of the body where the contents of the package (the supplement, such as Vitamin C) is finally delivered directly inside the cell. An example liposomal-Vitamin C supplement is included on the following page.

Vitamin C 1000mg as Ascorbic Acid
180 Tablets
Suitable for Vegetarians & Vegans
by Nu U Nutrition

On Amazon UK for £14.97

Liposomal Vitamin C supplement type



Optimized Liposomal Vitamin C SOFTGELS
China-Free
Quali®-C Scottish Ascorbic Acid
High Absorption
Immune System Support & Collagen Booster Supplement
Non-GMO
No Soy
30 Servings (90 softgel tablets but 3 is taken at a time to achieve a dose of 1000mg)

On Amazon UK for £22.97

Action for ME, welfare guides

Source: www.actionforme.org.uk/living-with-me/welfare-benefits

If you have M.E. or care for someone who has M.E., you may be entitled to claim welfare benefits. Action for M.E. produces a range of factsheets about the benefits available, including information on applying and, if necessary, appealing. You can find links to these below.

- ESA: an overview (Updated 13 November 2018, replacing our two previous ESA factsheets)
- Supporting evidence for PIP and ESA claims (Please be aware this is currently under review)
- PIP: an overview (Updated 13 November 2018, replacing our previous PIP factsheets)
- Universal Credit: an overview (Updated 13 November 2018, replacing our previous Universal credit factsheet)
- Permitted Work
- DLA: a guide to filling in the form
- DLA: revisions and appeals
- DLA face-to-face medicals for adults and children
- DLA for children under 16
- Blue Badge (Please be aware this is currently under review)

If you need help applying for Employment and Support Allowance or Personal Independence Payment, you can use SEAP's benefit support app. This helps you prepare by testing any application form answers you have drafted to estimate how many points you might score.