Long Covid and Post Viral Fatigue - Ref165

with Dr. Gerald Coakley

20th May 2021

TRANSCRIPT

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Steven Bruce
I'm joined today by Dr. Gerald Coakley. Dr. Gerald Coakley is a consultant rheumatologist. He's been one of those for 20 years. So he specialises in things like rheumatoid arthritis, septic arthritis and all that sort of stuff, as well as ME, chronic fatigue syndrome and post viral fatigue. Gerald, great to have you with us. This is not a new thing for you, is it, fatigue? This goes back a little bit longer than COVID. So how did you get into fatigue in the first place?

Dr Gerald Coakley
Yeah, well, thanks very much for the invitation to to come and talk to everyone. Yeah, so it's one of the oddities about fatigue is it isn't really anybody's specialty within medicine. People go to medical school dreaming of being a surgeon or anaesthetist or radiologist or cardiologist, and they don't go thinking, Oh, I want to specialise in fatigue. So it's one of the common concerns or complaints that patients have when they develop fatigue is who do I see about it? It doesn't really fit neatly into anybody's specialty. And so what's tended to happen is that disparate groups of professionals have got involved over the years, so often endocrinologists because there's a concern could it be an underactive thyroid that's making people get fatigued, or infectious disease doctors, because fatigue often follows infections, or psychiatrists, because often when people have got unexplained fatigue problems, it affects their mental health and so they develop anxiety and depression, and rheumatologists are another group. So as you said, I'm rheumatologist mostly I'm dealing with arthritis, lupus, and that kind of thing. But I got involved in fatigue not long after I became a consultant, actually, about 20 years ago. I was invited to join a small group, an interdisciplinary group working in the private sector, specialising in people with fatigue and fibromyalgia. So I worked with psychiatrists, psychologists, physiotherapists, and I was a physician. And my job was to sort of do the due diligence and make sure that there wasn't a physical health problem giving rise to the fatigue. And so I was just invited in as a team member and I found it really fascinating. I really enjoyed working with psychiatrists and psychologists and I learned a lot from them. And that a company that folded, basically. And when it did, I just kind of really missed working in that group. And so I decided to set up my own little group in 2007, getting some of those different disciplines together and trying to help people with chronic fatigue syndrome, ME, which I've been doing now for the last 13, 14 years.

Steven Bruce
That intrigues me actually, and I know we're intending to talk about post viral fatigue on this particular show, but if someone goes to a GP with something which is manifesting itself as fatigue, how does the GP know who to send them to given that you've already said psychiatrists, endocrinologist, rheumatologists, and probably lots of other specialisations could be involved?

Dr Gerald Coakley
Well, so there is guidance about what to do. So the National Institute for Health and Care Excellence, NICE, produced a guideline in 2007, to try and help GPs to address this. And it sort of set out the ways in which ME or Chronic Fatigue Syndrome can present and set up the sort of normal investigations that a GP should do to rule out other disorders like an underactive thyroid or diabetes, or celiac disease or inflammatory muscle disease, kidney and liver disease, and so on. So it set out a list of things that should be done. And then it said, so then you advise, the GP can advise a patient about how to pace and how to sort of deal with the symptoms of fatigue. And if they're not getting better after two or three months, the advice is to refer them on to an interdisciplinary fatigue service. And there are services of that sort

around the country. They're often not very well funded, they're often difficult to access. A lot of them have been closed down over the last few years. There's also been a lot of controversy over whether the treatments they offer is effective. So it's a real patchwork and particularly for there's a subgroup of people with ME or Chronic Fatigue who are very severely affected and are house bound or in worst cases, even bed bound, and there isn't really any provision for people in that category. There's nobody really who's to set up to cater for that. And actually, numerically, it's quite a large group. And if you imagine being bed bound for months or years, and nobody can help you, that's not a good position to be.

Steven Bruce
We might, we might return to that later, particularly if I get questions on it. But I know that much of the interest today is focused on long COVID, so called, but do you want to lead us into that? I mean, whether long COVID, the same as post viral fatigue and so on?

Dr Gerald Coakley
Yeah, well, that's a really good question. And the answer to that question is, nobody's really sure at the moment. And almost certainly, well, it's already clear that long COVID or post COVID-19 syndrome, is in fact, not one thing, it's a number of different problems. Presenting with the common feature that patients so affected do not get better within the expected timeframe so that they're 4, 6, 8 weeks later, they've still got symptoms.

Steven Bruce
Isn't that the same for any post viral syndrome?

Dr Gerald Coakley
Yes, but it's complicated in COVID and I'll try to explain why. So we've known that if you think about classical post viral fatigue syndromes, which we see most commonly with Epstein-Barr virus that causes glandular fever, for many, many years, it's been known that one in five people, typically teenagers or people at university, who get glandular fever, one in five of them will have a persistent fatigue problem for months after glandular fever. And there are actually lots of infections that can do that, it's not just Epstein-Barr virus, various different viruses, some bacterial infections, some tropical infections. So there's quite a number of conditions that present like this. But what's different about COVID? I mean, in some respects, you're right, it’s similar, but in other respects, it is quite different. So obviously, one of the main differences with COVID is that it kills huge numbers of people throughout the world. And we don't see that with EBV, Epstein-Barr virus, or most of the other infections I've been talking about. So as well as causing flu like symptoms, it can also cause inflammation in the body, in the lungs, in the heart, in the brain, in the gut, it can lead to hyper inflammatory syndromes and intensive care and death. So it's clear that it is quite heterogeneous or pleiotropic, in its effects, this virus, and some of the people who have got ongoing fatigue symptoms, or other physical symptoms, tingling, numbness, or pins and needles, chest pains and so on, have got serious, ongoing organic damage in their bodies and that's why they feel as they do, they have lung fibrosis or scarring or cardiac fibrosis. And that is different from what we see in classical post viral fatigue, where, as far as anybody knows, there's no issue with ongoing viral reputation or viral damage. It's something a bit more complicated than that. And so when I think about this problem, I think of it really into two sort of distinct categories. So there's the older multimorbid person who's probably got physical damage from the virus, and that may be why they have ongoing symptoms.

And there's the younger previously fit and healthy person who gets a minor COVID illness, but then has a fatigue problem which persists for weeks and months afterwards. And I think, in people under the age of 40, by and large, what we're seeing is what I would regard as classical post viral fatigue of the sort that we see in Epstein-Barr virus and we manage it in a similar way. And so I think it's different in the older age group. But that does introduce some problems, I think, for the younger people, because a lot of the younger clients that I see are really worried that the reason they've got post viral symptoms is because they've got serious organ damage, heart damage, brain damage, and things like this. So they're worried that they're going to never recover from this. And that makes the problem worse. I mean, so it's not to say that it's a psychological condition because it's an infection, but if you're very worried and anxious about the situation and worried that you're never going to recover from it, of course, it's going to make the situation more distressing than it would otherwise be. So quite a lot of what I spend my time doing is just reassuring people that it's appropriate, that actually there isn't any serious underlying disease to account for their symptoms. This is what we see in post viral fatigue syndromes. And we knew how to help people with that, because we've done been doing it for years.

Steven Bruce
Are able yet to come up with any figures on the incidence of post viral fatigue in COVID, as opposed to other syndromes?

Dr Gerald Coakley
Yeah, well, so significant ongoing fatigue that's more than just a few weeks, more than a month or six weeks, is seen in about 5%.

Steven Bruce
And is that more or less or the same as every other post viral fatigue?

Dr Gerald Coakley
It's pretty similar actually. It's a bit less than we see with EBV, it's probably a little bit less than we saw with SARS, where it is about 15-20%. But we're still working it out. You'll see lots of different figures around, so the Office for National Statistics came up with a figure of 1.1 million, I think, and that was in December, just before the second wave hit. And if you take that figure, then that's a lot more than 5%. But if you take, for example, Tim Spector at Kings, has given a figure of 5% having symptoms for more than six weeks, and that's based on his cohort, which is about 1.5 million people logging in their symptoms every day. So I don't think we have a final figure, but it's some it's somewhere around 5-10%, something of that nature.

Steven Bruce
Yeah. Actually, Joanne's sent in a question asking, but doesn't flu also kill 1000s of people when flu is at its worst, so therefore, isn't that very similar to COVID? Particularly in the big epidemics that we saw in decades gone?

Dr Gerald Coakley
Yes, that's true. But flu, if flu's going to kill you, it'll kill you and that's over and done with. What we don't see with flu is that people have a many months stay on ITU, develop end organ damage, and things like

that. You either with flu pretty much don't survive it, and it's usually the very elderly who get that, or it's a nuisance and you're better in a week or two. So I think COVID is different. You don't see, for example, the hyper inflammatory problems and the clotting problems with flu that we do with COVID.

Steven Bruce
Okay. Is it a silly question to ask how we would recognize post viral fatigue in a patient? Given that many of them will be coming to us for other reasons and may have it?

Dr Gerald Coakley
Well, I suppose the hallmark of post viral fatigue, or particularly as it evolves, if it goes on for more than three or four months then that's when we tend to label it chronic fatigue syndrome. And the hallmark of that is what's called post exertional malaise. So in most people doing some physical activity, doing some physical exercise, will make you feel better, will make you feel more refreshed and more energetic. Whereas in post viral fatigue and chronic fatigue syndrome, quite characteristically and unusually and in fact, to the extent that if you don't have this feature, you don't have it, part of the definition is that fatigue will get worse after activity, be that physical or mental. So if your patient has that, then it could well be post viral fatigue or ME and if they don't have this feature of symptoms getting worse after activity, then they can't have the condition. And one of the difficulties is that for some people, the onset of fatigue is quick, within hours of doing exercise, but for other people, it's delayed by a day or two. On the day, I feel fine but two days later, I can't get out of bed, and I'm in bed for four or five days. That but that would be what I would look forward in confirming the diagnosis.

Steven Bruce
I suppose also written on the tin must be you can't have post viral fatigue unless you've had the virus. So is it the case that if you had a relatively asymptomatic dose of COVID, you could have a nasty post viral fatigue syndrome?

Dr Gerald Coakley
Yes, unfortunately it is. So it's a very difficult area and a bit of a moving target. So if we just think pre COVID for a minute and we see patients coming in with new onset fatigue. The problem is that the symptoms of ME or chronic fatigue syndrome are very similar to the symptoms of flu. And you can get ME or chronic fatigue syndrome through things other than infections, you can get it through stress, through burnout, various kinds of mental health crises can provoke it. And so it can be really difficult to be sure whether somebody has actually an infection triggering the thing or not. And it's one of the advantages we have with this COVID pandemic, there's not many advantages, but one of them is that we knew pretty much for sure, certainly anyone who got COVID, after about July or August of 2020 will have definite proof that they had it. There's a whole load of people who got the infection in March or April last year, who think they had COVID but the testing wasn't available at that time and so we can't be sure. And generally, the approach that we've been advised to take is to assume if somebody got ill in March or April last year with some kind of viral illness and they're not improving, we assume that it's COVID. But yes, there are absolutely people who have really trivial infection.

Steven Bruce
If you took blood tests, in those patients, presumably you'd still see antibodies, wouldn't you? Which would be an indication that they'd had it?

Dr Gerald Coakley
Well, unfortunately, not necessarily. So there are some people who don't mount antibodies. And also, I mean, I know because I spend most of my time in an NHS hospital and we're all having tests all the time and so I've got colleagues in the department I work in who had PCR proven COVID, who had antibodies, and then two or three months down the line, they don't have antibodies anymore. So the antibodies are usually in most people, you are right, they do hang around and one of the ways you can tell that somebody has had an infection is by doing an antibody test, but they're not totally reliable and there are people who have had an infection and they're antibody negative.

Steven Bruce
Does that call into question the value of the vaccines if there are people, I don't know in what scale they might appear, but people who don't preserve their antibodies?

Dr Gerald Coakley
Well, no, I think is the short answer. But I think it's one of the reasons why viruses were developed, and even people who've had a COVID infection, they're still advised to get a vaccination is because the longevity of antibody response after vaccination, particularly with the two doses is much better than after a natural infection.

Steven Bruce
I see, right. There was quite encouraging news today, I think, wasn't there, that I think they've found that 100% of those vaccinated twice did produce antibodies in the Pfizer and the Oxford vaccines, I think.

Dr Gerald Coakley
Yeah, I think it's 96%. Yeah, but pretty much. It's really, I think, very much better than we reasonably were hoping. Because you look at the effectiveness of a flu vaccination, the cover is much less impressive. So it really hit the jackpot, all the vaccines, in terms of effectiveness.

Steven Bruce
Epstein-Barr has raised some interest amongst people, Christina says, is there a link between it and fibromyalgia in later life?

Dr Gerald Coakley
Well, not that I'm aware of. I mean, the problem with Epstein-Barr virus is that if you look in the general population, the population prevalence of having antibodies to EBV is about 70-80%. So most people will have antibodies. And when something is so prevalent as to be almost universal, it's very hard then statistically to work out whether it's influencing your risk of getting fibromyalgia. I think it would be fair to say that the majority of people who have EBV do not get Fibromyalgia because just most people don't have fibromyalgia.

Steven Bruce
That might actually answer a question from Vladimir, who says he keeps hearing that EBV is to blame for so many things and he wants to know if there's any truth in that, but it sounds to me as though there's association but no causation in this?

Dr Gerald Coakley
Yeah, I think there were years when people were researching ME, chronic fatigue syndrome, when there was a real interest for decades in the idea that it was to do with persistent viraemia, persistent sources of Epstein-Barr virus, and that somehow persisting virus was causing the symptoms and I think that's been completely disproved. And so, basically what you get with EBV, most people who get it are asymptomatic, they're completely unaware of it, but there's a subsection who get glandular fever, swollen glands, sore throat, malaise for a few weeks and some of them go on to get chronic fatigue but most of them don't. The other thing that you can get is EBV is one of those viruses that does remain within the body. It's not got rid of and it remains within the bone marrow, a bit like herpes simplex does, and so if later in life you become immunosuppressed, because you develop a lymphoma or leukemia or because you're immunosuppressed because of an autoimmune condition, then the EBV can escape the control of our immune system and it can cause serious problems. But that's extremely rare. It can cause bone marrow aplasia and this kind of thing, but numerically, it's tiny. It's like 0.01% of people who get that. So in the main EBV is pretty much a non event, I think, as far as we currently understand.

Steven Bruce
Okay. As I said earlier on, we are here more to talk about long COVID post viral fatigue than we are other things, and there are quite a few questions coming in about vaccines and things now because I raised them. But I want to get back to the main subject. Elspeth's asked a question, how does one deal with fibrosis of the heart and lungs? She says, how do you deal with it, but it may not be you personally.

Dr Gerald Coakley
There are interdisciplinary teams that deal with this because it's very complicated. So with difficulty, I think is the thing to say, it's not easy to treat scarring of the lungs, it's not easy to treat scarring of the skin or scarring anywhere, really. So sometimes, there's a degree of reversibility. And there are some, certainly the early experience with patients who've got inflammation and scarring of the lungs due to COVID is that steroids can be really effective. But we know from the studies that were done in the in the UK during the first wave of COVID, that dexamethasone, which is a form of steroid, can be really helpful in reducing the serious effects of COVID, but also for those people who've got lung scarring, it can really help healing post discharge. So my researcher colleagues tell me that they use steroids quite liberally and they can be very effective. I think that's all, I mean, you can get scarring in the lungs due to things like autoimmune disease, inflammatory disease, and in those situations, we use immunosuppressants as well as steroids, thus far, I don't think we have any evidence in COVID that that's a sensible thing to do. But certainly, I think my experience has been that quite a few of the post COVID consequences you see, as in people who develop inflammatory disease and these kind of scarring problems, they can respond really well to short courses of steroid and that's mostly what we use,

Steven Bruce
What does the rest of the treatment package comprise when you're dealing with post viral fatigue?

Dr Gerald Coakley
Well, I guess the steps are, one is the physician-y bit which is what I do, the due diligence. So my job is to make sure when people have got lots of symptoms, because typically, your post viral fatigue sufferer will not only describe fatigue, they'll describe lots of other symptoms like problems with memory, thinking, word finding, which is often called brain fog, problems with concentration, they'll have problems like palpitations, shortness of breath, abdominal pain, abdominal upset, tingling, pins and needles, numbness. So they have lots and lots of symptoms and they are very often, because it feels very odd having all these symptoms suddenly, so not unreasonably, they will fear that they've got some terrible multisystem disease that's eating away at their bodies. And the first question you need to try and answer is, have you or have you not got some terrible thing that's eating away at all your organs. And that's really the role of the physician, I think, is to sort of work that out. So I'm taking the history, doing examination, doing appropriate and judicious tests. So we don't test everybody endlessly but we do what seems proportionate in testing to the situation. So if it's a 20 or 30 year old person who's previously fit well, we're probably not going to investigate very much. And if it's someone who spent three months on ITU with COVID, you're probably going to investigate quite a lot because the likelihood of you finding something is different in those two groups. So that's the first bit, just working out what's going on here, doing some prudent testing to check kidney and liver function, all these kinds of things. So that's what we do. And then mostly what I spend my time doing is just explaining to people why it is that people get post viral fatigue and that it's normal to have lots of physical symptoms when you've got post viral fatigue, this is just what we see and we always have, we did pre-COVID and we have post-COVID, as well. And so we try and develop a sort of model with the patient for them to understand why it is that they're experiencing these symptoms to try and normalize them to make them seem less frightening. We do an assessment of their psychological health, because very often it's affected. And you have to be quite sensitive about this, because people often think that you're sort of saying they're being hypochondriac or they're imagining it. And it's absolutely not about that. It's just about trying to get a holistic assessment of how they are and that means you've got to assess their soul as well as their body, if you see what I mean. And then in terms of what you do next, you basically give people advice and support, it's about saying, if you manage this period right, these next few weeks and months, there's a good chance you'll get better. What does that mean? So it means, first of all, being optimistic, having a reasonable expectation that you will get better because that's what happens with most people, not catastrophizing, not spending a lot of time thinking, oh, woe is me, my life is over, I'm never going to get well again. Not, I'm afraid, in the main looking at Facebook groups and that kind of thing, which unfortunately, in my experience, often just give people the heebie jeebies and make them worry, they're never going to get better. And then we give advice on pacing. So that's your energy is less than it used to be, you've been had an infection, you're not doing well, so you've just got to cut down your activities to something that you can cope with. So that you can get a consistent pattern of activity and rest, avoiding boom and bust, where you feel a bit better one day and you do more and then you spend days in bed, this is a cycle you've got to get rid of. So we talk to them about pacing, we talk to them about, very often what we find is that these patients have got major problems with sleep, they can't sleep or they're sleeping too much. They're sleeping up half the day as well as much of the night, and both of these are unhelpful. And so we try and explain why that pattern is not helpful and is likely to perpetuate their problem. And often we find that people are very anxious and that's understandable, but actually it can make the situation worse. So one aspect of what we do where appropriate is if people have developed disordered sleep patterns, are sleeping too much or too little or they're very anxious or panicky, then we'll get a psychologist involved to help them deal

with that. And it can be hugely beneficial quite quickly, it's surprising how quickly we see people turn around. And then the other approach is really one of rehabilitation. So that's where I involve other members of the interdisciplinary team and really from my point of view, the clinical specialists who are best at rehabilitation are occupational therapists. So they are in a team members who really specialize in getting someone who because of a health problem is no longer able to function as they used to. It doesn't really matter whether that's because you've had a virus or because you've had a leg amputated or you've had a stroke or whatever. If something's happened to you catastrophically or suddenly, that means that you were two or three months ago functioning normally and now you can hardly get out of bed. How do you turn that situation round? Well, you do it cautiously, slowly, with care and compassion, with guidance, supported by somebody who's helped other people recover from a situation like that, and that's what occupational therapists do. For many people, it's just about giving advice and reading material think you'll be alright, get on with it. And then where people have got lots of sleep problems or anxiety and depression problems, then I recommend psychological therapy. And for people where that's not the case, then it's more a sort of rehabilitation occupational therapy gradual increase of physical activity types of thing.

Steven Bruce
Gerald, given the NHS system is under a lot of pressure at the moment and I speak to so many people who are not able to get an appointment with their GP, where's the cut off for us as chiropractors, osteopaths, physios, if a patient comes to us and they're complaining of things like those that you've described, where's the cut off where we can give them advice along the lines of, it's going to get better, we know this, we recognize this, but at some point, we have to say, no, you need to get a referral, so you need to go see your GP. Or should we not? Should we just say, we think you've got post viral fatigue, go see your GP anyway?

Dr Gerald Coakley
Oh, well, I think it would depend on when you're seeing them. So I think if it's early days, if you're seeing someone who's a month or two after having COVID, and they're still feeling under the weather, I wouldn't regard that as at all surprising. And I don't see any reason to sort of get in a panic about that, either for the therapist or the patient. If you're getting up to three or four months, or someone is very severely affected, and they can't get out of bed, then I think you think, this is this is a serious problem or they're really not recovering at the rate they should be and then they should go and see their GP in the first instance, because the GP will have access to an array of services, including the new long COVID clinics that are being set up in the NHS.

Steven Bruce
Okay. Jennifer's asked about chronic fatigue, which you mentioned before, you said it could go on for months after a viral infection, but she asks if it can relapse and remit over years, if it's not managed or treated?

Dr Gerald Coakley
Absolutely, it can, it can and it very often does. And unfortunately, it can even if it is appropriately managed and treated. Unfortunately, total recovery from ME or chronic fatigue is probably the exception rather than the rule. So what I usually say to people is, I think if you've got these people relatively severely

affected, then it is usually with treatment, feasible to expect people to get their life back on track and perhaps back into work and doing normal activities, but it's very often the case that they may not make it back to full time work, they may not make it back to the kind of exercise levels they were doing before and they may just have to lower their expectations of what they can achieve. And it's likely that in periods of stress or if they get another infection or whatever, they may have a setback and that's not particularly to be surprised about or upset about, because that's just what happens, unfortunately. But I will say there are some cases and particularly if you see people early on, they got post viral fatigue, they haven't yet gone and developed a chronic problem that's gone on for months and months, I think it'd be more optimistic. But certainly, if they've had symptoms for 9, 12, 18 months the likelihood of total recovery forever and ever is probably is quite low.

Steven Bruce
Is there any sort of lifestyle advice that you would offer people before they get to a stage where they need medical intervention? Pip has asked whether probiotics are helpful at all in managing post viral fatigue? Something like that?

Dr Gerald Coakley
Well, I don't think there's a lot of evidence about that, I think certainly making sure that you're getting adequate, I think lifestyle adjustments is important, making sure you're getting adequate rest, making sure you're not over exercising, making sure that you're managing stress appropriately, making sure that you're making time for pleasure. What I often see is that people's energy level have gone down and they put all of their energy and focus into what they see as the most important thing, for example work. And then they have no energy or time to do anything else, to shop, to see people, to exercise, to have to have any pleasure. And unsurprisingly, that is not sustainable for a long period. And sometimes you have to sort of cut down on everything a bit, including work, to try and give yourself time to maintain a balance in your life while you're recovering.

Steven Bruce
Okay, getting off that topic a little bit. I don't know who's asked this question, but someone asked what we know about T cell immunity and COVID-19. And I remember reading a bit about this sort of, I think early on last year, about T cell immunity.

Dr Gerald Coakley
Yeah, so when you when you think about the response to a virus, the early response is driven by T cells. So we have CD4 and CD8 cells, which are both T cell subsets, and CD8 cells their job is to fight viruses. That's what they do. So the initial recognition of a virus is based on a T cell response. And so our ability, unfortunately to do anything about the T cell response is a bit limited except through vaccination. So vaccination will allow your immune system to recognize peptides or epitopes on the virus and so they will prime the T cells to be able to recognize the virus when it comes into the body. And the other thing they will do is the T cells will help the B cells, which produce antibodies, to produce antibodies against the virus, or at least antibodies against the vaccine, which will help provide protection. So you kind of need both bits to get your immunity, both the T cell response and the B cell response. One of the reasons why there's been a lot of interest in this is that it's possible, and this is speculative, but it's possible that in different individuals which bit of the immune system is activated in response to COVID may have an

influence on whether you develop a post viral fatigue syndrome or not. It's conceivable that some people might have, for example, a strong T cell response and they clear the virus and they don't get post viral fatigue, whereas other people may have a weaker T cell response and take longer to clear the virus and it may cause more trouble and perhaps result in more long COVID features. But we don't know the answer to this yet. There are a few silver linings to the cloud that is COVID and one of them is that the NIH in the states has put $1.3 billion of research funding into looking at this very question. And it's about a quarter of a billion in the UK has gone into it as well. So I think I think the questions are very pertinent and I think in a year or two's time, we will have much clearer answers to those questions. But right now, we don't really know.

Steven Bruce
We've only got a minute left. So one more question, if I may. I don't know who's asked this, but the question is, do ENT issues arise first, then giving brain inflammation, which then relays into other systems of the body?

Dr Gerald Coakley
Yeah, well, I mean, the virus obviously gets in through the nose or the mouth, so that's the way it gets in. It seems then to go to the because it attaches to these ACE2 receptors, angiotensin converting enzyme receptors, which are mostly in the lungs, actually, that seems to be where they get in. And then subsequently, there is evidence that in some individuals, they go to the brain, it seems to be really rare but there are certainly some studies that were published in Queen Square, the National Institute for Neurology and Neurosurgery, of patients getting encephalitis from COVID. But it's like it's about 0.1%. So we're not sure in the generality, there's a very vigorous blood brain barrier, which stops viruses from getting into the brain usually, and I haven't seen data yet to be sure whether it really is getting into the brain. But it does seem to be first of all, nose and throat and then into the lungs and then it goes around to parts of the body to the ACE2 receptor.

Steven Bruce
Brilliant. Gerald, thank you. I know you've got a clinic this afternoon and most of our viewers will also have patients arriving shortly, if not already. So thank you very much for your time. Thank you for that. I hope it's reassured some of our people that we know something if not everything about long COVID and post viral fatigue syndrome.