

## Long COVID and female hormones

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### What is long COVID?

Long COVID is defined as symptoms that persist for more than 3 months after having the COVID-19 infection. There are people who contracted COVID-19 in the first wave and they're still feeling unwell many months later.

Common symptoms of long COVID include fatigue, discomfort or being unwell after exertion, joint and muscle pains, brain fog, headaches, chest pains, palpitations, cough, breathlessness, irritable bowel symptoms, skin rashes, low mood and irritability and this list is not exhaustive. Symptoms commonly fluctuate and can come and go in the so-called 'Corona-Coaster'.

About 1.5 million people in the UK currently have long COVID<sup>1</sup>.

### What is perimenopause and menopause?

The menopause is when the ovaries stop producing eggs and the production of the hormones estrogen, progesterone and testosterone fluctuates and then falls. When this happens, it can cause a wide range of unpleasant symptoms such as hot flushes, night sweats, memory problems, fatigue, reduce stamina, brain fog, muscle and joint pains, low mood and anxiety. The hormones stay low forever which results in a raised risk of developing certain diseases such as osteoporosis, heart disease, diabetes and dementia.

Medically, the menopause is defined as the point in time when you haven't had a period for more than 12 consecutive months; on average this is at age 51. The perimenopause is the time leading up to this when hormones fluctuate and start falling, and symptoms begin to emerge with periods still occurring, even if irregularly.

The perimenopause can last for many years and most commonly affects individuals in their 40s but some people enter an early menopause (under 45 years) or have Premature Ovarian Insufficiency (if under 40 years).

The perimenopause and menopause cannot always be diagnosed by hormone levels as these can really fluctuate over time.

### What is the link between long COVID and the peri/menopause?

Long COVID affects women far more commonly than men, and women aged 40-60 are at the highest risk of being diagnosed with long COVID (although there's no diagnostic or definitive test for long COVID). These findings are causing researchers to question if there's a link with female hormones and long COVID. It's worth noting that not only does there appear to be a link between long COVID and the peri/menopause, there are many women who are peri/menopausal (and have long COVID) who have never been offered treatment for their low hormones due to the peri/menopause.

Many women with long COVID are experiencing changes in their periods in terms of frequency, how long they last for, or how heavy or light they are. For some, their periods stop altogether. Many of the symptoms of long COVID overlap with and are similar to those commonly experienced in peri/menopause. Individuals with long COVID experience fatigue, headaches, dizziness, poor concentration, brain fog and memory problems and, if the sufferer is female, symptoms are often likely to be due to low estrogen and testosterone levels.

A study by Newson Health Research and Education found that around one third of women with long COVID reported changes in their periods since having the COVID-19 infection<sup>2</sup>. This study also showed that 77% of women find their long COVID symptoms get worse just before their period, which is the time in a normal monthly cycle when estrogen levels are at their lowest.

## COVID-19 infection and effects on the ovaries and hormone production

Any infection has the potential to affect the function of the ovaries, and this could potentially lead to a worsening of perimenopausal and menopausal symptoms if the individual is at this stage in life. It is likely however, that the COVID-19 infection is affecting women's ovaries more severely than other common infections and it appears to be having a more severe effect on the production of hormones such as estrogen and testosterone.

There are receptors in the body known as angiotensin-converting enzyme 2 (ACE2) receptors which the COVID-19 infection binds to to enter the cell. There are many of these ACE2 receptors in the ovaries so this is a likely reason why so many women experience more severe perimenopausal and menopausal symptoms when they are infected with COVID-19 – it appears that the COVID-19 infection really takes hold in the ovaries. The knock-on effect of this is the ovaries don't function at their normal levels and less hormones are produced as a result; estrogen in particular is then produced in lower quantities than before, and this is what may cause many of the symptoms to occur.

A sudden drop in these hormones may trigger a more sudden, or a more severe perimenopause or menopause than would have been the case had the woman entered perimenopause naturally.

Most commonly a woman in her 40's and 50's will have low female hormone levels and their ovaries become more vulnerable and less likely to recover from infections, especially COVID-19. For this reason, long COVID symptoms due to low estrogen and testosterone levels tend to persist unless women are given the right dose and type of Hormone Replacement Therapy (HRT), which often includes testosterone replacement as well as estrogen.

## Improving long COVID and peri/menopause symptoms

Emerging research and clinical experience is suggesting that many women benefit from taking HRT when they first experience the COVID-19 infection (there has been shown to be a reduced mortality rate of over 50% in women if they were already taking HRT) and when suffering with long COVID.

Starting HRT can be useful to determine which symptoms are due to low hormone levels, and which symptoms might be unrelated to low female hormones and therefore require an alternative management strategy.

HRT is a very effective, safe treatment for peri/menopausal symptoms, and it also has long term health benefits such as reducing the risk of cardiovascular disease, osteoporosis (bone weakening disease), depression, dementia, bowel cancer and even early death. HRT most commonly involves replacing the hormones estrogen and progesterone, and there are various types and ways to receive the hormones.

Many women with long COVID and peri/menopausal symptoms also benefit from taking testosterone replacement. Women produce around 3-4 times more testosterone than estrogen from their ovaries when they are young but levels of testosterone also fall significantly when ovarian function is affected.

Testosterone can be particularly useful to treat low mood, fatigue, brain fog, muscle weakness and joint pains. Your healthcare professional will be able to advise whether this is an option that might be of benefit to you.

The hormonal imbalance induced by the COVID-19 infection can be a major barrier to recovery for women suffering with long COVID. Estrogen is known to have many anti-inflammatory effects, and it is possible that HRT may also help to treat other long COVID symptoms, even those that are not directly linked with estrogen deficiency.

## Other barriers to recovery from long COVID

Individuals suffering with long COVID need to look at their whole lifestyle, routines and overall wellbeing. Here are some factors that should be addressed (as well as taking HRT) in order to maximise recovery from long COVID.

**Nutrition and gut health:** it is normal and helpful for there to be trillions of bacteria in the gut. They help digest food and absorb nutrients. Some bacteria are 'friendly' and help digestion and absorption in the gut and some bacteria trigger unhelpful reactions and are sometimes referred to as 'harmful' bacteria. The balance and composition of friendly and harmful bacteria is known as the gut 'microbiome'.

Evidence is showing that COVID-19 is having a detrimental effect on the gut microbiome by reducing the number of friendly bacteria and increasing the harmful bacteria. Ongoing changes to the microbiome can result in symptoms such as diarrhoea and bloating and the bacterial imbalance may also be contributing to inflammation elsewhere in the body. Low estrogen due to peri/menopause can also contribute to a worsening of the gut microbiome and lead to similar symptoms.

Making changes to your diet can often improve symptoms whether you have long COVID, peri/menopause or both. Aim to eat a wide variety and amount of plant-based foods per week (fruit, vegetables, nuts and seeds), eat fermented foods such as sauerkraut, kimchi and kefir yoghurt, increase your intake of fibre, and take a probiotic supplement. This can all help restore your microbiome into a 'happier' balance, and relieve abdominal bloating, cramps, constipation and diarrhoea.

**Improving your sleep routines:** problems sleeping well are very common in both long COVID and the peri/menopause. And poor sleep often worsens other symptoms such as fatigue, brain fog, anxiety and low mood.

It is important to maintain good habits that help your sleep such as going to bed and getting up at the same time every day (including at weekends). Avoiding caffeine in the afternoons and evenings may help, as will reducing or cutting out alcoholic drinks. Some moderate physical exercise on a daily basis and reducing screen time, especially in the evenings, can often be beneficial. Magnesium supplements can improve sleep and over-the-counter remedies to aid sleep can be tried too.

If you are still struggling to sleep despite all the above, your doctor may be able to prescribe medication such as melatonin, or a low dose of a sedating antidepressant such as amitriptyline.

**Helping your mood and emotional wellbeing:** if you have long COVID, you may feel low or anxious for many reasons. These include the stress of living through a pandemic, not being able to sleep and feeling exhausted, having a chronic illness with multiple symptoms and maybe feeling uncertain about the future. You may not be able to work or look after your family, and any financial issues due to not being able to work can be a huge stressor.

On top of this, the COVID virus itself can have a direct effect on the brain and cause neurological symptoms including changes in mood and emotional wellbeing. Low hormone levels are also a very common cause of anxiety and depression, changes to your confidence and self-esteem, reduced motivation and drive and a general feeling of not being yourself.

HRT can often be very effective at improving these types of symptoms. If you are struggling, it is important to seek help from your healthcare professional and also talk to family or close friends about how you're feeling.

**Over work and overexertion:** trying to do too much too soon, both physically and mentally, can cause a worsening of long COVID symptoms ('boom and bust'). It can be very frustrating for people who are used to being busy and active to slow down and pace themselves. But it is very important to establish how much activity you can tolerate without making yourself feel unwell, and then set realistic goals and

gradually increase your activity levels. The Royal College of Occupational Therapists has produced some helpful advice about this: <https://www.rcot.co.uk/conserving-energy>

Addressing and improving all the factors above, including taking HRT, gives individuals the best chance for a full recovery from long COVID.

Here is an account of a woman with long COVID who wasn't aware she was also perimenopausal:

I caught COVID on March the 23rd, 2020. My husband and daughter were also unwell but whereas they recovered in a week or so, I didn't. I was suffering from fatigue, muscle aches, brain fog and breathlessness. I just couldn't seem to shake it off. I kept trying to resume my normal life but I felt completely wiped out. Despite only leading 25% of my previous active lifestyle, I was having to take to my bed for several days every couple of weeks. I was horrified at how much I was sleeping and my daughters got used to returning home from school to find me sleeping deeply on the sofa.

At my lowest point I couldn't even climb one flight of stairs. I took myself to A&E but they shrugged me off and said I would eventually get better. I attended a long COVID clinic but they were at a loss as to why I was so fatigued. They reassured me I wasn't alone and advised me that many women in my age bracket were suffering with similar symptoms, but they couldn't do anything to help.

I began to feel desperate, depressed and anxious. A simple dog walk left me exhausted and crashed out on the sofa. But I looked well. My family and friends became impatient with my constant fatigue. Wasn't it time I got help for my depression? But I knew I wasn't depressed.

In September 2021, I was discharged from the long COVID clinic. I was in despair. I was 48, I couldn't go shopping with my daughter, I was unable to walk up a steep hill. I walked past my gym where I used to cycle and swim and wondered, 'would I ever be able to go back?' I couldn't contemplate cancelling my gym membership –, that would be admitting defeat. But I still couldn't even cook a family meal without having to lie down.

I started to read about women using estrogen to fight long COVID symptoms. I was intrigued. Could this help me? In October 2021, I saw a private long COVID specialist. I had a blood test and the next morning the consultant phoned. "I know why you are feeling so terrible" he said, "you have no estrogen or testosterone in your blood". He started me on estrogen gel and referred me to a menopause specialist.

Within ten days I felt better. I dropped my mid-day nap. My brain fog disappeared and I could actually complete a sentence. I no longer crawled into bed at 9.30pm and I didn't wake up feeling as though someone was lying on top of me. It was like a grey cloud had been lifted. I still cannot believe how much the estrogen replacement has transformed how I feel. I feel brighter, more positive, my fatigue is manageable. I feel my old self again. After 18 long months, I have even started going back to the gym. My only regret is how long it took to be prescribed the HRT. I am so frustrated that over 18 months, I had 9 blood tests, and not one doctor checked my hormone levels. I could have started HRT months ago and I would have regained my life so much sooner.

## References:

1. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK. Office for National Statistics, March 2022. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/3march2022>
2. Newson, Louise & Lewis, Rebecca & O'Hara, Margaret. (2021). Long Covid and menopause – the important role of hormones in Long Covid must be considered. *Maturitas*. 152. 74. 10.1016/j.maturitas.2021.08.026.

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