

Long COVID, diet and hormones

This booklet is co-authored by Dr Sarah Glynne and Emma Ellice-Flint. Sarah Glynne is a GP and menopause specialist, and Emma Ellice-Flint is a clinical nutritionist with a special interest in the menopause.

This booklet has been written to compliment the 'Long COVID and female hormones' factsheet which is available on the balance website.

The purpose of this booklet is to explain poor gut health and the microbiome, and outline what can be done to improve your gut health through practical advice, including a dietary strategy for patients with histamine intolerance.

Long COVID

There are currently 1.5 million people living with long COVID in the UK¹, and this number is predicted to rise as the virus continues to circulate. Long COVID is associated with symptoms that affect multiple organ systems. Many people with long COVID are unable to go about their daily lives in the usual way, and their ability to care for their family and work is often affected. 1 in 5 long COVID sufferers have not returned to work since they contracted COVID-19, and many more have only been able to return to work in a reduced capacity².

As yet, there is no cure for long COVID, so a broad approach is used that targets several different factors influencing individual symptoms and the amount or rate of recovery achieved by an individual. These factors include hormone imbalance (which can be effectively treated with hormone replacement therapy) poor gut health, poor sleep, mood disturbance, overwork and overexertion.

Gut health

People with long COVID are often advised to optimise their 'gut health' to improve their chances of recovery. But what does this actually mean? Why does it matter, and what can be done to improve the health of your gut?

Poor gut health also occurs in the peri/menopause; women at this stage of life are the group most likely to get long COVID and are therefore at higher risk of having poor gut health. This is why taking steps to improve your gut health is particularly important if you are peri/menopausal and have long COVID.

The health of your gut is also important because, along with the menopause, poor gut health is associated with long term health conditions such as cardiovascular disease and dementia. Making healthy changes to your diet and taking HRT will not only improve your long COVID symptoms, they both bring long term benefits to your health.

What is the gut microbiome?

The human microbiome is the complex ecosystem of microorganisms that lives on and inside your body. Within your gut, there are approximately 100 trillion different microbes, mainly bacteria, that have many important functions, such as:

- · helping digestion
- · producing important nutrients
- energy (glucose and fat) metabolism
- · regulating activity of hormones including estrogen
- · boosting the function of the immune system

A healthy microbiome consists of a large number of different types of bacteria, particularly beneficial bacteria that perform the functions listed above.

An unhealthy microbiome is less diverse, has fewer beneficial or 'friendly' bacteria, and has a higher number of 'unfriendly' bacteria. This unhealthy combination is known as **dysbiosis**, and it can cause symptoms such as constipation, diarrhoea, bloating and flatulence. It has also been linked to many long term health conditions including obesity, diabetes, heart disease, inflammatory bowel disease, arthritis, certain cancers, autism, depression and Alzheimer's disease.

Causes of an unhealthy microbiome (dysbiosis)

Your diet has a major effect on the composition of your microbiome – your own unique mix of friendly and unfriendly bacteria. Plant-based ingredients are generally high in fibre, which nourishes the friendly bacteria. Plant-based ingredients also contain phytochemicals (chemicals that give food its colour, taste and aroma). Phytochemicals have antioxidant and anti-inflammatory properties, and they positively influence the gut microbiota. A typical 'western' diet is low in fresh plant-based, fibre-rich ingredients but high in sugar which feeds the 'unfriendly' bacteria and high in processed foods – both of which can lead to dysbiosis.

Smoking, a lack of exercise and certain drugs such as antibiotics can also cause an unhealthy gut microbiome.

Estrogen and the gut microbiome are closely linked³. The estrogen produced by your ovaries is metabolised by gut bacteria that help the hormone be reabsorbed and re-

circulated in the body. Plant-derived estrogen and the 17- β estradiol type that is produced naturally in the body promote a healthy gut microbiome. After the menopause (if HRT is not taken), the lack of estrogen can cause dysbiosis³.

Lastly, an unhealthy gut microbiome can result from infections, such as COVID-19.

The microbiome and COVID-19

Here are some facts that research has revealed so far about the gut microbiome and $\frac{\text{COVID-19}}{\text{COVID-19}}$

Individuals with acute COVID-19 infection frequently experience gastrointestinal symptoms⁴, occurring in up to 85% of patients².

Dysbiosis is common in people with COVID-19 and has been linked with more severe disease⁴.

A healthy plant-based diet and probiotic supplements are associated with a lower risk of getting COVID-19, and/or results in less severe disease⁵⁻⁸.

Following a COVID-19 infection, individuals with unhealthy gut microbiomes are more likely to develop long COVID⁹.

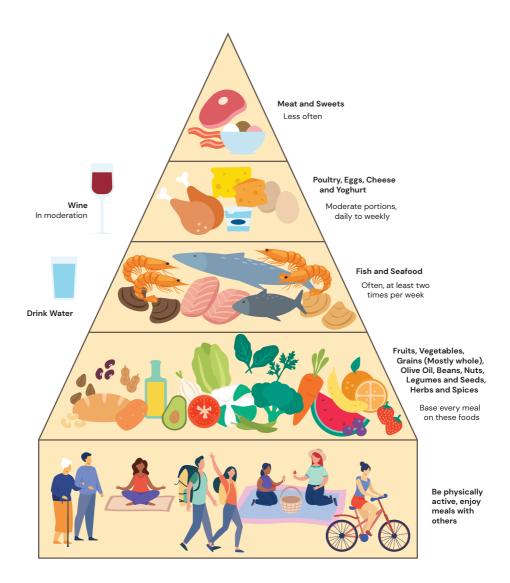
Long COVID is associated with ongoing negative changes in the microbiome9.

A small study showed that treating long COVID patients with a supplement containing probiotic strains of lactobacillus and inulin (a type of fibre found in chicory), reduced both gut and non-gut symptoms such as cough, fatigue and general wellbeing¹⁰. The addition of a phytochemical-rich food capsule containing powdered extracts of citrus fruit, turmeric, aloe vera, pomegranate and chamomile, resulted in even greater symptom improvement¹¹.

While more research is needed to learn about the full effects of dietary manipulation in people with long COVID, these early studies suggest that poor gut health may increase your risk of catching COVID, and developing long COVID, and is also a barrier to recovery from long COVID.



The Mediterranean Diet Pyramid¹²



The Mediterranean Diet is one of the healthiest diets in the world. It can reduce your risk of obesity, diabetes, cardiovascular disease, dementia and some cancers¹³. It may also reduce hot flushes and night sweats, and improve your mood and bone health, if you are peri/menopausal^{14,15}. For these reasons, it is the diet recommended by the British Heart Foundation, Diabetes UK, The Stroke Association, The Alzheimer's Society and the European Menopause and Andropause Society.

The Mediterranean diet is plant-focussed, and therefore rich in fibre and phytochemicals such as polyphenols. Polyphenols reduce inflammation, which reduces the risk of chronic diseases ¹⁶. Plant-based fibre 'feeds' the beneficial gut microbiota, resulting in a richer, more diverse microbiome. Fish, nuts and seeds (like flaxseed and Chia seeds) contain Omega 3 oils, which also promote a healthy microbiome and have anti-inflammatory effects ¹⁷. Recently, the PREDICT study demonstrated that the food we eat has a direct effect on the composition of our microbiome, which influences our metabolism and overall health ¹⁸.

Fruit and vegetables also contain important vitamins and minerals, for example, berries and citrus fruits contain vitamin C which is a natural antioxidant and antihistamine.

Variety is key

Professor Tim Spector, co-founder of the COVID Symptom Study App and co-author of the PREDICT study, advises us to try to eat 30 different plant-based ingredients per week¹⁹. Different plants contain different types of fibre and phytochemicals, that support different gut microbes.

Eating a varied plant-based Mediterranean diet is the best way to encourage a diverse, healthy microbiome.

Try and avoid excess saturated fats (found in dairy, poultry and red meat), and reduce refined sugars and artificial sweeteners and processed foods, as these are all linked with dysbiosis, chronic inflammation and poor health outcomes.

Gradually increasing the amount of plant-based ingredients that you eat and making small beneficial changes can often result in noticeable improvements to gut health and the quality of your life.

Prebiotics and probiotics

Prebiotics supplements can further benefit your gut health; these are indigestible fibres found in many plant-based foods, that enter the large bowel and are selectively fermented by 'friendly' bacteria such as *Lactobacilli* and *Bifidobacteria*. This stimulates the growth of the 'good' bacteria, leading to improvements in your health²⁰. Prebiotics are only found in small quantities in your diet, so the amount you take in can be increased by taking a supplement. Examples include inulin (naturally found in chicory), and partially hydrolysed guar gum (PHGG, derived from guar beans).

Probiotics are foods or supplements that contain live 'friendly' microbes such as Lactobacilli and Bifidobacteria. They can be consumed by eating fermented foods that are rich in live bacteria. Examples include: sauerkraut (fermented cabbage), kimchi (Asian-style fermented cabbage with chilli), kefir (fermented yoghurt), kombucha (fermented tea), live yoghurt, aged cheese, apple cider vinegar, and fermented soy bean products (like miso, tempeh, or tamari). Probiotics don't last long in the gut, so it is better to eat little and often.

Alternatively, probiotic supplements can be taken to improve or restore the composition of the microbiome. (While there are many on the market, very few have been used in clinical trials).

Be aware...

Sometimes, it can take a while to see an improvement after you've made positive changes to your diet but stick with it and you will see the results in time.

If you have long COVID, you may find your symptoms get worse when you initially increase the amount of fibre in your diet, or you introduce fermented foods or a probiotic supplement, for example. If this happens to you, you may be suffering from histamine intolerance.

Histamine intolerance and long COVID

Some patients with long COVID will also have symptoms of histamine intolerance – this is characterised by low activity of an enzyme that normally breaks down histamine. Histamine intolerance is more common in women and if you have it, you may find it more difficult to optimise your gut health because many of the foods that are recommended are also high in histamine.

This is also why some women feel unwell when they start HRT because estrogen stimulates the release of histamine. Women with histamine intolerance can still have HRT, but it requires a different approach.

There is a booklet on histamine intolerance in more detail available on the balance website. When foods rich in histamine are consumed, the histamine builds up and causes symptoms that mimic an allergic reaction (many allergic symptoms are histamine related). These allergic symptoms include flushing, hives, diarrhoea, palpitations, headaches, wheeze, runny or blocked nose, and dizziness.

Many people with long COVID, especially women, have symptoms linked with histamine intolerance. It is possible that COVID-19 is triggering Mast Cell Activation Syndrome (MCAS) in these individuals. This is a condition in which the mast cells are hyper-reactive, releasing histamine at a faster rate than it can be broken down.

Many of the plant-based foods recommended to patients with long COVID to improve their gut health, are high in histamine, such as avocados, tomatoes, strawberries, bananas, nuts and pulses. Fermented foods, and some probiotics, have a particularly high histamine content and many individuals with long COVID find their symptoms flare up when they try to introduce these foods. This is particularly likely if you also have a pre-existing histamine intolerance – which you may or may not be aware of. Irritable bowel syndrome and undiagnosed food intolerances can be due to an underlying histamine intolerance.

If this sounds familiar to you, a modified approach is necessary when making dietary changes, to reduce symptoms of histamine intolerance while also improving your gut health.

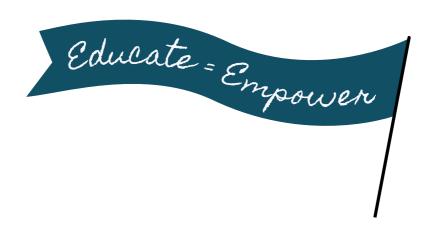
Improving gut health with long COVID when histamine intolerant

The degree to which histamine intolerance is contributing to your long COVID symptoms, and the rate at which you metabolise and break down histamine is unique to you. If you think (or know) you may be histamine intolerant and want to improve your gut health, the first step is to identify specific foods that trigger your allergic symptoms.

Keep a food and symptom diary for at least 4 weeks, to identify patterns and triggers for your symptoms. A diary template can be downloaded at the following link: https://www.histamineintolerance.org.uk/about/the-food-diary/

Having established a pattern between certain foods and your histamine intolerance symptoms, it is then necessary to change your diet, to avoid the trigger foods. Initially, eliminating alcohol, tea and coffee may be enough to relieve your symptoms, especially if combined with medications and supplements that are known to be of benefit (see 'Other things to try'). However, some of you will still have significant symptoms, and will need to adopt a more structured low histamine diet (see table in the appendix for histamine content of foods).

Once your symptoms have improved, you can slowly start to reintroduce foods into your diet to try to optimise your gut health.



Top tips on making diet changes if histamine intolerant:

- Introduce one new food at a time, every few days. This will help to reduce the risk of a symptom flare up, allowing the microbiome to adapt and the healthy bacteria to flourish.
- 2. Choose low histamine foods that are rich in prebiotics and polyphenols. Examples of low histamine, prebiotic foods include artichokes, asparagus, blackcurrants, carrots, cauliflower, red onion and brown rice. PHGG powder can be added to low histamine smoothies. A teaspoon of psyllium husk can be stirred into porridge. Examples of low histamine foods that are rich in polyphenols include: blueberries, broccoli, ginger, pomegranate, red cabbage, red onion, sweet potato and turmeric.
- Gradually add in higher histamine-containing foods in a step-by-step approach; fermented foods should be introduced later. The probiotic Saccharomyces Boulardii (SB) may be of benefit.
- 4. If symptoms get worse, go back a step and wait until you feel better. Then try again later or try an alternate plant-based ingredient.

If you are struggling, it is important to seek the support of a qualified dietician or nutritionist.

Other things to try:

Antihistamines

One study showed that 72% of people with long COVID who were treated with antihistamines reported a clinical improvement²². Loratadine (started at 10mg twice daily), can be purchased over the counter. Famotidine (40mg at night) is an antihistamine that binds to a different type of histamine receptor. Most people with long COVID and MCAS benefit from taking both types of antihistamine together. Famotidine needs to be prescribed by your healthcare professional.

Vitamin C

Vitamin C (250mg three times daily) is a natural antihistamine.

Diamine oxidase capsules

Some patients find that DAO capsules can reduce symptoms of histamine intolerance if taken 30-60 minutes before a meal

Other ways to further improve gut health

Aside from making helpful dietary changes there are other factors to consider to ensure a full approach is used to improve your gut health and, in turn, your long COVID symptoms.

HRT

Research shows the lack of estrogen at menopause can contribute to an unhealthy gut microbiome, and this is linked with increased inflammation and poor metabolic health, ultimately leading to an increase in the risk of obesity, diabetes and cardiovascular disease.

The peri/menopause can involve sleeping problems, less physical activity due to joint and muscle aches and pains, fatigue and lack of energy, and craving sugary foods. All these factors independently increase the risk of future chronic health problems, and they also cause poor gut health³. The good news is that dietary changes at and after menopause can improve gut health and reduce menopausal symptoms²⁴.

Postmenopausal women who take HRT have healthier microbiomes, reduced visceral fat, healthier blood sugar and blood cholesterol, and reduced inflammation compared to postmenopausal women who don't take HRT^{3,23}. HRT also improves sleep quality and ability to exercise which can in turn lead to further gains in your gut health.

HRT effectively treats symptoms due to a lack of hormones such as estrogen, and these are very common in women with long COVID. HRT may also help reduce symptoms that are not directly caused by estrogen deficiency, due to its anti-inflammatory properties.

However, taking replacement estrogen may exacerbate symptoms of histamine intolerance. If you notice an increase in your allergic symptoms when starting HRT, it is important to speak to your healthcare professional to ensure that you are prescribed the correct dose and type of HRT.

Sleep

A good night's sleep is associated with a healthy microbiome so anything you can do to improve your sleep will help ward off dysbiosis.

The key factors that promote a good night's sleep are having a consistent bedtime routine – going to sleep and waking up at the same time every day – and to keep your bedroom cool and dark.

Eating plenty of protein and complex carbohydrates with the evening meal helps to regulate blood sugar levels and reduces the risk of snacking, which supports healthy gut microbiota. Eating natural digestives such as herbs and spices, apple cider vinegar, lemon and lime juice, garlic and chilli, also improves sleep quality. Herbal teas such as chamomile, L–Theonine, and magnesium 500mg daily, are calming and sleep-inducing.

Over-the-counter sleep aids may be helpful. Stimulants such as alcohol, caffeine and sugar all disrupt sleep and should be kept to a minimum.

If you are still struggling to sleep, you should see your healthcare professional who may prescribe melatonin SR (2-4mg at night), or a low dose of amitriptyline. Sleeping tablets are generally not helpful.

Exercise

Exercise enhances the composition of our microbiome and has many long-term health benefits. It also promotes a good night's sleep.

However, without treatment, many people with long COVID will not be able to exercise. Trying to exercise too soon or doing too much exercise can actually make long COVID symptoms worse.

Perimenopausal women may find that taking estrogen and testosterone helps them to feel less fatigued, improves their mood and motivation, reduces joint and muscle pains and improves muscle strength. As women start to feel better, they can undertake light exercise such as walking and yoga, and gradually increase their physical activity depending on their exercise tolerance.

Smoking

Smoking has a detrimental effect on your gut health as well as your general health and should be avoided.

Take home messages

A rich, diverse microbiome is essential for good health and wellbeing, and reduces the risk of future chronic diseases. Individuals with long COVID are more likely to have dysbiosis and poor gut health and many factors contribute to this.

Evidence is now suggesting dietary changes can increase the diversity within your gut microbiome, improving your gut health, and helping your recovery from long COVID.

A Mediterranean style diet is rich in plant-based foods that improve the composition of the microbiome, reduce inflammation in the gut, and ultimately reduce the risk of chronic inflammatory diseases. Early research suggests this type of diet may help people with long COVID too.

Using a Mediterranean style diet approach to improve gut health and symptoms of long COVID may need to be modified for individuals showing signs of histamine intolerance.

Hormone imbalance is an important barrier to recovery for many long COVID patients.

Estrogen and testosterone replacement (HRT) effectively treats symptoms due to a lack of these hormones, and estrogen may also improve other symptoms as it has anti-inflammatory properties, boosts immunity, reduces dysbiosis and improves gut health.

The relationship between COVID-19 infection, histamine, the microbiome and hormones is complex. More research is needed to assess the effectiveness of HRT and changes to diet in individuals with long COVID.

Resources and References

Balance website

Factsheet - Long COVID and Female Hormones
Booklet - Histamine Intolerance (HIT)
Article - 5 Reasons to Boost Your Gut Health
Podcasts - Dr Louise Newson podcast, episode numbers 012, 016, 040, 047, 120 and 137

Emma Ellice-Flint website

https://emmasnutrition.com. This site includes links to Low Histamine and Fermented Food workshops and the cookbooks, The Happy Hormone and The Low Histamine.

Additional resources

Book - The Real Mediterranean Diet: A practical guide to understanding and achieving the healthiest diet in the world by Dr Simon Poole. Published by Cambridge Media Group.

Podcast - ZOE Science and Nutrition

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Histamine levels in types of food and drink

Food Groups	Low Histamine	High Histamine	Note
Vegetables	All fresh vegetables except →	Avocado, Aubergines, Tomatoes, Spinach, Rocket, Mushrooms. Pickled & canned vegetables.	The fresher the vegetables the better. Possibly peas may cause symptoms.
Fermented Vegetables & Pickles	No	Sauerkraut and other fermented vegetables. Pickled vegetables.	Including fermented vegetable sauces e.g. soya sauce, miso.
Fruit	All fresh fruit except →	Strawberries & raspberries, plums, citrus (oranges, limes, lemons, grapefruit).Tropical fruit e.g. papaya, banana, pineapple, kiwi.	Avoid over ripe fruit.
Dried Fruit	Only dried fruit that has NO sulphur dioxide & preservatives.	Dried fruit with sulphur dioxide, sulphites & preservatives should be avoided.	Including food made with dried fruit such as fruit mince, unless it definitely has NO preservatives/sulphur dioxide added
Grains, flour	Only gluten free grains and flours e.g. rice, oat, corn, quinoa, potato, millet, amaranth, teff, kamut, hulled buckwheat. Einkorn ancient wheat flour is ok.	All gluten grains e.g. wheat, barley, rye, spelt. Sourdough & Yeast, usually found in breads.	Avoid sourdough bread even if gluten free. Gluten free soda bread is ok. Spelt grain/flour may be ok.
Legumes & Pulses	No	chickpeas, beans, soy, lentils, butter beans, navy beans, black beans, red kidney beans, black eyed beans, peas etc.	This includes avoiding dips containing legumes/pulses e.g. humus and soy products such as tofu.
Nuts and seeds	Only macadamias, pistachios & chestnuts, Tiger nuts. 1-2 Brazil nuts/d. Pumpkin, hulled hemp & chia seeds. Psyllium husk.	Most nuts and peanuts, most seeds inc flax/linseeds.	Including nut butters & spreads.
Dairy	Only fresh dairy e.g. fresh milk, cottage cheese, quark, fresh curd, fresh mozzarella/ bocconcini, ricotta.	All fermented dairy foods from cow, goat, sheep.	Including yoghurt, kefir, fermented cheeses, sour cream. Butter is low histamine if uncultured/unfermented.

Food Groups	Low Histamine	High Histamine	Note
Dairy alternatives	Plant milks are ok, even if they are made from nuts/seeds. Rice or oat milk, fortified with calcium, is the most suitable.	Fermented plant foods e.g. coconut yoghurt, soy yoghurt, oat yoghurt.	Take care with vegan cheeses as they may contain artificial colourings & preservatives. Use only natural coconut milks/creams without gums/preservatives.
Fats	Extra virgin olive oil, ghee, rapeseed oil, coconut oil, unfermented/culture free butter.	Fermented/cultured butter, soy oil, nut oils. eg sunflower oil.	Fresh unfermented/ uncultured butter is ok.
Meat, Poultry, Eggs	Freshly cooked fresh meats & poultry; Fresh eggs may be ok. Carefully frozen meat is ok.	Cured, smoked & aged meat e.g. bacon, salami, hot dogs; Possibly mincemeat if not fresh.	Aged fresh meat is also high histamine, very fresh meat is ok. Egg whites may be less tolerated.
Seafood	Freshly caught fish except →	Mackerel, mahi-mahi, tuna, sardines, herring, anchovies. All shellfish and crustaceans/molluscs. All smoked fish. All canned fish.	Including avoiding all canned, pickled and smoked seafood.
Sugar, Sweets & Chocolate	Sugar & Sweets are ok except →	Chocolate, cocoa, cacao, carob and sweets that contain sulphur dioxide dried fruit & nuts/seeds.	Sweeteners such as honey, cane sugar & maple syrup are ok. Not artificial sweeteners & malt extract.
Seasonings, Condiments & Herbs	Fresh & dried herbs, spices, clear distilled white malt vinegar, salt, a little pepper. Homemade vegetable stock & homemade freshly made, or from frozen, white fish stock.	Other vinegars, mayonnaise, tomato ketchup, pickles, olives, capers, soy sauce, miso, fish sauce, tamari, Marmite, Vegemite, cumin. Excess garlic. Yeast extract, flavour enhancers (glutamate, sodium glutamate), bouillon, broth, animal/poultry stocks.	Including avoid heavily salted/seasoned food. Take care with hot spices - cayenne, chillies, curries - keep dishes mild.lf not using veg/ fish stock immediately after making, then freeze in portions & use from frozen.
Teas & Coffee, Drinks	Herbal tea, including Rooibos tea, Tumeric tea, Ginger tea, Fennel tea, Chamomile tea.	Green & black teas, Yerber Mate, Coffee, Kombucha, kefirs & other fermented drinks. Tomato & tropical juice. Energy drinks. AVOID ALL ALCOHOL.	Including any drinks with artificial colours or preservatives. Avoid carbonated/soda drinks, inc sparkling water, as the carbonation can potentially aggrevate Sx.

Balance app and website

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Dr Louise Newson is a GP and menopause specialist and the founder of the balance app and website.

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