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*Managing Sleep  
Problems in People With*  
**LONG COVID**

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**I**n 2019, information regarding a fast-spreading atypical pneumonia-like illness began to be reported. The cause of the illness was a virus, now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In February 2020, the World Health Organization (WHO) officially named the disease caused by the virus as “coronavirus disease 2019” or more simply, “COVID-19.”<sup>1</sup> Its symptoms can be nonexistent, mild, moderate or severe and can manifest as a sore throat, congestion or runny nose, cough, diarrhea, fatigue, fever or chills, headache, muscle or body aches, nausea or vomiting, diarrhea, loss of taste or smell, shortness of breath or difficulty breathing, and chest pain or pressure. After recovering from the infection, approximately 40%–90% of people continue to have persistent symptoms or develop new symptoms such as “brain fog” (i.e., difficulty concentrating, confusion or forgetfulness) and changes in taste and smell that last for many months to years.<sup>2</sup> When symptoms persist for three months or more after recovery from COVID-19, a person is considered to have “long COVID.” Long COVID tends to affect people who have had severe COVID-19 but can affect people who recover from milder cases as well. People with long COVID frequently report problems with insomnia, although other sleep problems have been reported such as hypersomnia and sleep-disordered breathing (e.g., obstructive sleep apnea [OSA]).<sup>2-4</sup> However, sleep disorders are an overlooked problem in people with long COVID and little data exists with regard to managing sleep problems in this group.

## About COVID-19

SARS-CoV-2 enters the body primarily through the respiratory tract. Spike protein on the surface of SARS-CoV-2 attaches to the angiotensin-converting enzyme 2 (ACE2) receptor, which exists on the cells of organs such as the respiratory tract, heart, neurons and endothelium (i.e., inner lining) of blood vessels. After the virus interacts with the ACE2 receptor, it enters a host cell, replicates and causes the cell to release new viruses. This viral release destroys the host cell and causes the release of inflammatory chemicals (e.g., cytokines and chemokines) associated with cellular injury. Viral-related injury to central nervous system and respiratory system tissues may contribute to sleep problems after SARS-CoV-2 infection.<sup>5</sup> For example, viral-damage to the thalamus, brain stem and respiratory center in the brain may contribute to abnormal sleep-wake behaviors and sleep-disordered breathing, and viral-damage to the lungs may contribute to breathing problems associated with long COVID.

## COVID-19-Related Sleep Studies: What They Uncovered

Most research studies investigating sleep problems in people who recovered from COVID-19 have used surveys, which assess participants’ subjective perceptions of their sleep rather than using objective data to assess sleep problems. Thus, the data may not fully reflect what is actually occurring in people with long COVID and sleep problems. For example, a person may underestimate or overestimate the amount of time needed to fall asleep.

To counteract this drawback, Mekhael et al.<sup>3</sup> used an objective method – a wireless wearable wristband manufactured by Biostrap (Bradbury, California) – to collect sleep data of people with and without long COVID. The wristband was a photoplethysmography (PPG)-based device, which emitted specific wavelengths of light onto the skin. Light reflected from the skin was detected by a photodiode and used to measure blood vessel volume changes occurring with each heartbeat. This information was then used to determine heart rate, heart rate variability (i.e., variations in time between heartbeats), respiratory rate and oxygen saturation.

The sleep patterns of patients with a history of COVID and individuals who had never had the disease were compared. Sleep staging was based on heart rate variability rather than on electroencephalography (EEG) signals, and the stages were divided into “awake sleep” (i.e., the first stage of non-rapid eye movement [NREM] sleep), “light sleep” and “deep sleep.”

Mekhael found that sleep architecture was altered in patients with a history of COVID. Compared to individuals without a history of COVID-19, patients with long COVID had

less total sleep time, more awake sleep time, less light sleep time and less deep sleep time. This phenomenon was noted, regardless of disease severity.

## Long COVID, Insomnia and Managing Sleep

Patients with long COVID often complain of insomnia. In general, treating insomnia typically involves the use of sleep-inducing medications (e.g., benzodiazepines, barbiturates and hypnotics) and to a lesser extent cognitive behavioral therapy for insomnia (CBT-i). However, patients with insomnia, including patients with long COVID, often do not feel improvement with medication alone.

Identifying risk factors for poor sleep during and after contracting COVID-19 may be beneficial in alleviating insomnia and poor sleep after infection. Research has indicated that insufficient sleep or sleep disruption has a negative impact on disease severity and treatment outcomes.<sup>3,4</sup> Therefore, improving the sleep hygiene of patients with COVID-19 (e.g., reducing noise or light exposure, use of chronotherapy), including during hospitalization, may be helpful in improving treatment outcomes and reducing the effects of long COVID.

Early recognition by clinicians of sleep dysfunction in patients with long COVID and implementing multidisciplinary interventions may be beneficial. However, in clinical practice, general practitioners have insufficient information with regard to recognizing and managing sleep problems in patients with long COVID.<sup>6</sup> Guezguez and colleagues<sup>6</sup> suggest that unnecessary pharmacological prescriptions to treat insomnia and other sleep disorders could potentially be avoided if more general practitioners had information regarding sleep disorders in patients with long COVID and if a multidisciplinary team consisting of, for example, general practitioners and sleep specialists were utilized.

For patients with long COVID who struggle with insomnia, an alternative to

sleep-inducing medications may be melatonin, which is a sleep-inducing hormone that improves sleep onset and is typically used to treat circadian rhythm disorders. Melatonin and melatonin receptor agonist drugs (e.g., ramelteon) are believed to reduce respiratory problems via their anti-inflammatory and immune-enhancing effects,<sup>4,7</sup> which may also improve sleep quality. In addition, melatonin and melatonin receptor agonists may be beneficial in alleviating other symptoms of long COVID such as brain fog and pain.<sup>8</sup> However, the use of melatonin to treat sleep problems in people with long COVID has not been studied extensively and additional research would need to be conducted to know more.

## Integrative Medicine: A New Approach to Sleep Management

Integrative medicine may be a promising approach in treating sleep problems in people with long COVID. Integrative medicine focuses on treating the whole person rather than just alleviating symptoms. Thus, a treatment plan may involve pharmacological and nonpharmacological therapies to address different aspects of a patient's symptoms.

In a recent paper, Roth and colleagues<sup>9</sup> described their experience in successfully using an integrative health approach to treat two patients with long COVID. Their approach combined traditional medical management (e.g., drug therapy), nonpharmacological approaches (e.g., meditation) and behavioral and lifestyle changes (e.g., exercise).

Their first patient was a 48-year-old woman who recovered from a mild COVID-19 infection but had lingering symptoms of migraine headache, nonexertional shortness of breath without wheezing, episodic chest pain and palpitations, panic attacks and fatigue. She had been taking metoprolol for hypertension before contracting COVID-19, and in response to her lingering symptoms, her primary care physician recommended albuterol for shortness of breath, ibuprofen — as needed — for migraine headaches and alprazolam for anxiety. In their integrative approach, Roth's team prescribed a nasal steroid (fluticasone), amitriptyline for migraine, a lower dose of metoprolol, escitalopram for anxiety and referred her for psychotherapy. She was also prescribed a five-minute breathing meditation exercise and a daily 30-minute walk. At the one-month follow-up, she reported an improvement in her symptoms and the resolution of her shortness of breath. Palpitations and episodic headache and fatigue also improved.

The second patient was a woman who had recovered from COVID-19 seven months earlier. She had lingering symptoms of anosmia (i.e., total or partial loss of the sense of smell) and dysgeusia (i.e., impaired sense of taste), loss of appetite, a 20-pound unintentional weight loss, joint pain, brain fog and extreme fatigue. She also reported symptoms of excessive daytime sleepiness and snoring at night, for which she was referred for a sleep study. She was diagnosed with severe OSA and treated with continuous positive airway pressure (CPAP). She was also prescribed meloxicam (a nonsteroidal anti-inflammatory drug) and turmeric (a spice) to alleviate joint pain, a daily 30-minute walk and a high-calorie meal plan. At the three-month follow-up, she reported that her symptoms were gradually improving and she had stopped losing weight. She still experienced intermittent fatigue and cognitive deficits, but they were less frequent.

## Conclusion

Scientists are not sure why long COVID occurs. Reasons for long COVID that have been suggested are:<sup>9</sup>

- A chronic low level of inflammation in the brain, heart, muscle and nerve tissues.
- An autoimmune condition in which the body makes antibodies that attack the brain.
- Dysfunction of ACE2 receptors in the heart and lungs.
- A hypercoagulable state and endothelial dysfunction, which cause widespread immune response dysregulation.
- Decreased blood flow to the brain because of autonomic nervous system abnormalities.
- An undetectable reservoir of an infectious or noninfectious virus that continues to trigger an immune response.

## Sleep Hygiene Tips for Individuals With Long COVID

People with long COVID should foster habits that maintain consistent sleep-wake times, for example:<sup>2,6</sup>

- Create a sleeping environment that is conducive to sleep (i.e., comfortable environmental temperature, free of excessive lighting and noise);
- Maximize exposure to daylight, particularly morning light, to enhance daytime wakefulness;
- Avoid or reduce nighttime exposure to artificial lighting, including light emitted by phones, computers and/or television;
- Maintain a healthy diet and diet habits (e.g., avoid eating caffeine-containing foods before sleep);
- Get regular exercise (ideally outdoors and early in the day to get maximum light exposure);
- Engage in calming activities before going to bed such as reading a book or listening to music.

Individuals with long COVID and insomnia should avoid:

- Going to bed when not tired, which can cause a person to associate bed with wakefulness rather than sleep;
- Watching the clock while in bed at night, which can add to anxiety about "not getting enough sleep" and worsen insomnia;
- Participating in strenuous activity before bedtime, which can delay sleep onset;
- Eating a large meal before going to bed, which can delay sleep onset; and
- Playing video games or watching videos in bed, which can delay sleep onset.

More information is needed regarding the relationship between long COVID and sleep disorders; a better understanding of this relationship will allow more effective management of the overall health of patients with lingering symptoms of the infection. Additionally, a treatment approach that involves the input of several types of clinicians such as general practitioners and sleep professionals could potentially allow sleep problems in patients with long COVID-19 to be recognized and treated earlier, which could potentially reduce symptoms of long COVID. 🌙



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