

How Proper Sleep Lowers Infection

Analysis by Dr. Joseph Mercola

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STORY AT-A-GLANCE

- > Research shows sleep enhances the efficiency of T cell responses, allowing your immune system to kill foreign invaders such as viruses with greater ease
- Ga(s)-coupled receptor agonists such as adrenaline and prostaglandin which decrease during sleep — prevent immune cells from activating a sticky protein called integrin that allows the T cell to attach to the viral target
- > Higher levels of molecules that inhibit integrin activation are also found in malaria and cancer, for example, which suggests this pathway may contribute to the immune suppression associated with these pathologies as well
- > People who awaken during the first sleep cycle also tend to have lower levels of natural killer cells, and deep sleep has been shown to strengthen immunological memories of previously encountered pathogens
- > Previous research has found the circadian clocks of mice control an essential immune system gene that helps their bodies sense and ward off bacteria and viruses

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Previous research¹ has shown that sleep deprivation has the same effect on your immune system as physical stress. When volunteers stayed awake for 29 hours straight, their white blood cell counts were found to increase during the sleep deprivation phase.

This is the same type of response you typically see when you're sick or stressed. In a nutshell, whether you're physically stressed, sick or sleep-deprived, your immune

system becomes hyperactive and starts producing white blood cells – your body's first line of defense against foreign invaders like infectious agents.

Elevated levels of white blood cells are typically a sign of disease. In other words, your body reacts to sleep deprivation in much the same way it reacts to illness. Your immune system, in turn, plays a key role in controlling inflammation in your body, and if it's not working optimally, your ability to fight off the infection will be impaired. As reported by Science Daily:²

"Sleep improves the potential ability of some of the body's immune cells to attach to their targets ... The study,^{3,4} led by Stoyan Dimitrov and Luciana Besedovsky at the University of Tübingen, helps explain how sleep can fight off an infection, whereas other conditions, such as chronic stress, can make the body more susceptible to illness."

Ga(s)-Coupled Receptor Agonists Affect T Cell Activation

When your immune system senses a foreign invader, such as a virus, white blood cells known as T cells (among others) are dispatched. Sticky proteins called integrins allow the T cell to attach to the infected target and kill it.

Dimitrov and his team decided to investigate⁵ the effects of signaling molecules called Ga(s)-coupled receptor agonists. While these signaling molecules are known to have immunosuppressive effects, it was not known whether they might inhibit the activation of integrins in T cells specifically, which is what they sought to determine here.

What they discovered was that certain Ga(s)-coupled receptor agonists did indeed prevent T cells from activating integrins once the target was identified. Ga(s)-coupled receptor agonists exhibiting this effect included:

- Adrenaline and noradrenaline (hormones)
- Prostaglandin E2 and D2 (proinflammatory molecules)
- Adenosine (a neuromodulator)

Sleep Helps Your Body Fight Infection

Levels of adrenaline and prostaglandin are known to decrease during sleep, and both have been shown to suppress integrin activation, so the team continued their investigation by comparing T cells obtained from volunteers during sleep and during sleep deprivation (when the volunteers were kept awake throughout the night).

All of the volunteers were infected with cytomegalovirus, a mostly benign virus, as they tend to have higher amounts of antigen-specific T cells. As suspected, the T cells were found to have significantly higher integrin activation during sleep than during wakefulness.

Ultimately, the findings reveal that when you sleep, Ga(s)-coupled receptor activation is inhibited, and this is one important way by which sleep helps your body combat inflammation. According to Besedovsky:⁶

"Our findings show that sleep has the potential to enhance the efficiency of T cell responses, which is especially relevant in light of the high prevalence of sleep disorders and conditions characterized by impaired sleep, such as depression, chronic stress, aging and shift work."

Dr. Louis DePalo, a professor of medicine, pulmonary, critical care and sleep medicine at the Icahn School of Medicine at Mount Sinai in New York City, who was not involved in the study, told Reuters:⁷

"Multiple clinical studies have demonstrated that people who do not get quality or sufficient sleep are more likely to get sick after being exposed to viruses. This study demonstrates yet another molecular pathway where good quality and quantity sleep may lead to immune supportive effects via immune cells, called T cells."

Sleep Also Plays an Important Role in Cancer

Dimitrov also points out that many pathological conditions, including malaria infection and cancer, have higher levels of molecules that inhibit integrin activation, which suggests that "This pathway may therefore contribute to the immune suppression associated with these pathologies."⁸

Certainly, we know that tumor growth speeds up when you're sleep deprived. This has previously been attributed to suppression of melatonin, a powerful antioxidant known to combat cancer. As noted in the clinical review⁹ "Melatonin, Sleep Disturbance and Cancer Risk," published in 2009:

"The pineal hormone melatonin is involved in the circadian regulation and facilitation of sleep, the inhibition of cancer development and growth, and the enhancement of immune function. Individuals, such as night shift workers, who are exposed to light at night on a regular basis experience biological rhythm (i.e., circadian) disruption including circadian phase shifts, nocturnal melatonin suppression and sleep disturbances.

Additionally, these individuals are not only immune suppressed, but they are also at an increased risk of developing a number of different types of cancer. There is a reciprocal interaction and regulation between sleep and the immune system quite independent of melatonin.

Sleep disturbances can lead to immune suppression and a shift to the predominance in cancer-stimulatory cytokines. Some studies suggest that a shortened duration of nocturnal sleep is associated with a higher risk of breast cancer development ...

The mutual reinforcement of interacting circadian rhythms of melatonin production, the sleep/wake cycle and immune function may indicate a new role for undisturbed, high quality sleep and perhaps even more importantly, uninterrupted darkness, as a previously unappreciated endogenous mechanism of cancer prevention."

The Sleep-Stress-Immune Response Link

Other research has also demonstrated just how intimate and direct the connection between sleep and immune function is. For example, a 1998 study¹⁰ discovered that people who were more likely to awaken during the first sleep cycle also tended to have lower levels of natural killer cells (NKC).

Overall, the age of the patient was the greatest determinant of NKC level, but sleep disturbances were responsible for about 12% of the variance in NKC level.

Stress is known to interfere with immune system function and has been found to increase susceptibility to the common cold and slow wound healing. Lack of sleep is a stressor, causing the release of stress hormones, and this was thought to be one of the first studies to provide direct evidence linking sleep with the human stress-immune relationship.

Other research¹¹ suggests deep sleep strengthens immunological memories of previously encountered pathogens. In this way, your immune system is able to mount a much faster and more effective response when an antigen is encountered a second time.

Your Circadian Clock Is Tied to Your Immune Function

Another study,¹² published in 2012, found that the circadian clocks of mice control an essential immune system gene that helps their bodies sense and ward off bacteria and viruses. When levels of that particular gene, called toll-like receptor 9 (TLR9), were at their highest, the mice were better able to withstand infections.

Interestingly, when the researchers induced sepsis, the severity of the disease was dependent on the timing of the induction. Severity directly correlated with cyclical changes in TLR9.

According to the authors, this may help explain why septic patients are known to be at higher risk of dying between the hours of 2 a.m. and 6 a.m. According to study author

Dr. Erol Fikrig, professor of epidemiology at the Yale School of Medicine:13

"These findings not only unveil a novel, direct molecular link between circadian rhythms and the immune system, but also open a new paradigm in the biology of the overall immune response with important implications for the prevention and treatment of disease.

Furthermore, patients in the ICU often have disturbed sleep patterns, due to noise, nocturnal light exposure and medications; it will be important to investigate how these factors influence TLR9 expression levels and immune responses."

Other Consequences of Insufficient Sleep

Considering the key role sleep plays in your immune function, it's easy to see how poor sleep can cascade outward, affecting a wide variety of health conditions. But that's not all. Sleep also affects gene expression, hormone regulation and brain detoxification, just to mention a few, which further strengthens its importance.

Aside from lowering your immune function, making you more susceptible to infections and cancer, other health problems linked to insufficient sleep include but are not limited to:

Increased risk of neurological problems, ranging from depression to dementia and Alzheimer's disease¹⁴ — Your blood-brain barrier becomes more permeable with age, allowing more toxins to enter.¹⁵ This, in conjunction with reduced efficiency of the glymphatic system due to lack of sleep, allows for more rapid damage to occur in your brain and this deterioration is thought to play a significant role in the development of Alzheimer's.

Increased risk of Type 2 diabetes – In one study,¹⁶ "excessive daytime sleepiness" increased the risk of Type 2 diabetes by 56%.

Increased risk of obesity.

Increased risk of high blood pressure, heart attacks and cardiovascular disease – Research has demonstrated that women who get less than four hours of shut-eye per night double their risk of dying from heart disease.¹⁷ In another study,¹⁸ adults who slept less than five hours a night had 50% more coronary calcium, a sign of oncoming heart disease, than those who regularly got seven hours.

Increased risk of osteoporosis.

Increased risk of pain and pain-related conditions such as fibromyalgia – In one study, poor or insufficient sleep was the strongest predictor for pain in adults over 50.¹⁹

Increased susceptibility to stomach ulcers.

Impaired sexual function.²⁰

Increased risk of depression and anxiety (including post-traumatic stress disorder), schizophrenia and suicide — In fact, researchers have been unable to find a single psychiatric condition in which the subject's sleep is normal.

Premature aging by interfering with growth hormone production, normally released by your pituitary gland during deep sleep.

Increased risk of dying from any cause²¹ — Compared to people without insomnia, the adjusted hazard ratio for all-cause mortality among those with chronic insomnia was 300% higher.

Optimizing Your Sleep Can Help Stave Off Chronic Problems

There's simply no doubt that sleep needs to be a priority if you intend to live a long and healthy life. Anyone struggling with chronic disease — which is at least half of the

American adult population — would be wise to take sleep seriously, as it can have a significant impact, not only contributing to the problem but also counteracting any other healthy lifestyle strategies you're using to address it.

As a general guideline, seek to get right around eight hours of sleep every night. Anything below seven hours really starts to impact your health (if you're an adult). For many, this means forgoing night-owl tendencies and getting to bed at a reasonable time. If you need to be up at 6 a.m., you have to have a lights-out deadline of 9:30 or 10 p.m., depending on how quickly you tend to fall asleep.

The good news is there are many ways to improve your odds of sleeping well, even if you're currently struggling. I've listed my top suggestions gleaned from research and various sleep experts in "Top 33 Tips to Optimize Your Sleep Routine" and "Sleep – Why You Need It and 50 Ways to Improve It."

Sources and References

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