



Sleep, the Immune System and the Common Cold



Summary: Human clinical studies have shown that sleep deprivation affects the immune system and reduces the ability to fight infections.

- A retrospective study of shift workers revealed that those with irregular schedules or who work late shifts had a higher incidence of colds and flu than those working regular, daylight shifts.
- In a study looking at the effect of sleep deprivation on efficacy of influenza vaccination, the authors stated, "These results suggest that the response to influenza vaccination may be impaired in individuals with chronic partial sleep restriction" and "our findings support the concept that adequate amounts of sleep are needed for optimal resistance to infectious challenge."
- A third human clinical showed that those who on average slept fewer than seven hours per night for two weeks were three times as likely to become symptomatic upon inoculation with rhinovirus as those who averaged more than eight hours sleep two weeks prior to the infectious challenge.
- EpiCor® (500mg per day) has been shown to significantly reduce the incidence and duration of cold and flu-like symptoms in two studies, each with over 100 subjects. Consequently, it is likely that EpiCor would be a good addition to dietary supplement formulas designed to support sleep and help people with occasional, mild sleep problems.



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A significant portion of the US population suffers from inadequate or disturbed sleep. Shift workers, parents of young children, menopausal women and the elderly represent groups that often sleep poorly or less than seems ideal in order to function at their best. Recent studies have shown that people are sleeping less across society as a whole (Jean-Louis et al, 2000). It is commonly thought that poor sleep can affect our ability to stay healthy. It is also commonly observed that many illnesses apparently increase our need for sleep. In spite of these 'known' interactions between sleep and immune function, it is only in recent years that scientific evidence has emerged to support these notions (Bryant et al, 2004). Many studies show the effect of acute and chronic lack of sleep on immune indicators in animals and humans. However, both the immune system and sleep are very complex, so it is not surprising that some studies looking at particular immune molecules and reactive cells appear to be contradictory or demonstrate effects that change depending upon the length of sleep deprivation and the time frame in which the indicators are measured (Majde et al, 2005 and Ricardo et al, 2009).

Rats that are sleep deprived for 24 hours show a decrease in lymphocyte levels. After 21 days of sleep reduction the animals show not only reduced lymphocytes and white blood cell counts, but also exhibit a decrease in the weight of the spleen, a critical component of the immune system (Zager et al, 2007). The authors of this study stated that although a short period of sleep deprivation "causes minor alterations in some immune parameters, prolonged [sleep reduction] like that observed in a modern population on a daily basis, causes impairment of systemic circulation of leukocytes and quite possibly increases the susceptibility to infectious diseases." In contrast, it has been shown that sleep deprivation lasting from two to twenty days results in activation of some immune parameters (Everson et al, 2005). However, the authors of this report noted that even with this activation, the immune system in the study animals was not able to eradicate invading bacteria and toxins. This same laboratory had previously shown that five days of disrupted sleep caused bacterial invasion of body tissues that are normally sterile, including the liver, lung, kidney and spleen (Everson et al, 1993). The bacteria in these tissues had apparently translocated from the intestine, which typically serves as a barrier to infection.

It has been shown that changes occur in the predominance of various immune cells as we experience different phases of sleep (Bryant et al, 2004), and that nocturnal sleep causes the balance between T helper cell types to shift in favor of Type 1 cells (Th1) in humans (Dimitrov et al, 2004). Th1 cells secrete pro-inflammatory cytokines which support the innate immune response against foreign cells and toxins. Th2 cells, on the other hand, generally produce more anti-inflammatory cytokines and support an adaptive immune response. The adaptive response includes the production of antibodies by B cells that target specific antigens. The innate and adaptive immune responses are not independent and interact in complex ways to protect the body from illnesses. These results are supported by another human study that demonstrated the converse effect: poor sleep causes a shift in favor of Th2 cells (Sakami et al, 2002). In other words, the immune system's first line of defense (innate response) is compromised when sleep is compromised.

Natural killer (NK) cells are another part of the innate immune system. They are able to recognize self-cells that have been infected by a virus and induce it to self destruct in a process termed apoptosis. NK cells can also recognize self-cells that have been transformed (become malignant) and cause them to undergo apoptosis. Therefore, NK cells have a primary defense role in the immune system. Results from a study of 39 women indicated that disrupted sleep can result in a weaker response by NK cells and a slower recovery after an experimental stressor (Wright et al, 2007). Similar results were found in a study that measured changes in NK cell activity within individuals. Lower NK cell activity was associated with less reported sleep (Shakhar et al, 2007).

Lange et al (Lange et al, 2003) conducted a direct study on the effect of sleep on the immune response to pathogenic challenge by measuring the effect of sleep deprivation after immunization with Hepatitis A vaccine. The amount of anti-Hepatitis A antibody was measured repeatedly over 28 days and compared in subjects who were allowed to sleep normally after vaccination and subjects who were sleep deprived for 36 hours. Antibody levels were assessed for 28 days in both groups.

While the antibody response was low in both groups for the first eight days, at 14 days the titers were 44% higher in the control group compared to those who had been sleep deprived. At 28 days, the difference was 97%, indicating that there may be critical times when even brief sleep deprivation can have a prolonged effect on the immune system.

If we focus on studies looking at the effect of lack of sleep on incidence of cold and flu and other relevant clinical indicators, we find that there is a correlation that supports the common perception that lack of sleep renders us more susceptible to illness. For instance, sleep deprived mice were unable to fight respiratory tract infections even though they had been immunized against the same influenza virus (Brown et al, 1989). A review of the scientific literature reveals that several human studies have shown that sleep not only affects the immune system generally but specifically affects people's ability to fight cold and flu. A well-controlled, retrospective study of shift workers and the incidence of illness among these workers in The Netherlands revealed that those with irregular schedules or who work late shifts, which are known to adversely affect sleep habits, had a higher incidence of colds and flu than those working regular, daylight shifts (Mohren et al, 2002).

In a study published in the Journal of the American Medical Association (Spiegel et al, 2002) healthy men were restricted to four hours of sleep for four days and then immunized against influenza. The subjects were sleep restricted for two additional days then allowed to sleep twelve hours to recover. Ten days later, the antibody titer in this sleep deprived group was half that of the control group. The authors stated, "These results suggest that the response to influenza vaccination may be impaired in individuals with chronic partial sleep restriction" and "our findings support the concept that adequate amounts of sleep are needed for optimal resistance to infectious challenge."

A recent, prospective study on 153 healthy volunteers showed that those who on average slept fewer than seven hours per night for two weeks were three times as likely to become symptomatic upon inoculation with rhinovirus as those who averaged more than eight hours sleep two weeks prior to the infectious challenge (Cohen et al, 2009). Using a measure of sleep efficiency, defined as the number of hours asleep divided by the number of hours in bed, the investigators found that subjects with sleep efficiencies below 92% were five times as likely to contract a cold after inoculation with rhinovirus as those whose sleep efficiency scores were greater than 98%.

One consequence of our modern lifestyle is a trend toward fewer hours of sleep and indeed, chronic lack of sleep (Bryant et al, 2004 and Majde et al, 2005). The clear and emerging evidence that chronic sleep disruption adversely affects the immune system adds to the concerns of people who either do not get enough sleep or who may experience disrupted sleep. EpiCor®, a fermentation product derived from brewer's yeast, has been shown to affect immune system markers and to reduce the incidence of cold and flu. At a dose of 500mg per day it significantly reduced the incidence and duration of cold and flu-like symptoms in a twelve week study of 116 people who had recently received influenza vaccine (Moyad et al, 2008). Similar benefits were observed in a subsequent study of non-influenza-vaccinated individuals (Moyad et al, 2010). In both studies the subjects were randomized to either receive 500mg of EpiCor or placebo once daily. Treatment with EpiCor significantly reduced the incidence of colds or flu-like symptoms. The duration of the symptoms was reduced from 4.25 to 3.59 days, but these data were not significantly different. Adverse events did not differ significantly between the treatment and placebo groups in either study and no adverse changes in blood parameters were associated with taking EpiCor.

EpiCor has also been studied in in vitro investigations. A study published in 2007 evaluated the immunomodulatory effects of EpiCor using a number of experimental models of immune system function and reported that EpiCor affects many immune system components. This study showed that treatment with EpiCor activated both natural killer cells and B lymphocytes, components of the innate and adaptive immune systems, respectively. EpiCor also demonstrated anti-inflammatory and antioxidant activities in these cell-based assays. Taken together, this in vitro and in vivo data suggest that EpiCor would be a good addition to dietary supplement formulas designed to support sleep and help people with occasional, mild sleep problems.





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