# Sleep Dysfunction and T Cell Polarization Patterns

Sleep dysfunction drives and is driven by inflammation, and impacts T cell polarization

**Cogence Clinical Pearl**

In this Cogence clinical pearl, we look at a remarkable paper on the impact of chronic inflammation on sleep dysfunction, and the way sleep dysfunction triggers changes in T cell polarization patterns, making the patient vulnerable to infection.

## *What the research says…*

This paper, from *Nature Reviews Immunology,* shows that **normal sleep promotes Th1 response,** via upregulation of IL-12 and interferon gamma (IFNγ). **Acute inflammation also increases Th1 response, so that any infection that might be causing the inflammation can be cleared.**

**Chronic inflammation and stress chemistry can both drive sleep dysfunction,** with loss of sleep efficiency, decreased sleep time, decreased slow wave sleep, and increased REM sleep. **These chronic sleep changes upregulate Th2 response and increase infection risk.**

## *Application…*

This paper shows, in remarkable detail and clarity, that disturbed sleep shifts the patient away from adequate Th1 status into Th2 dominance. So many patients are Th2 dominant for a variety of reasons (see the list of instigators of Th2 dominance behind the TOOLS tab on the Cogence member website). This paper links chronic inflammation & chronic stress chemistry production with this core tendency toward The dominance and inadequate Th1 response, through the mechanisms of sleep disturbance and sleep deprivation.

This is a remarkable paper that everyone should read from front to back.

## *The Research…*

**Sleep and inflammation: partners in sickness and in health.**
Irwin MR. Nat Rev Immunol. 2019 Nov;19(11):702-715.
*(color and bold added)*

**Abstract**
**The discovery of reciprocal connections between the central nervous system, sleep and the immune system has shown that sleep enhances immune defences and that afferent signals from immune cells promote sleep.** One mechanism by which sleep is proposed to provide a survival advantage is in terms of supporting a neurally integrated immune system that might anticipate injury and infectious threats. However, in modern times, chronic social threats can drive the development of sleep disturbances in humans, which can contribute to the dysregulation of inflammatory and antiviral responses. In this Review , I describe our current understanding of the **relationship between sleep dynamics and host defence mechanisms, with a focus on cytokine responses, the neuroendocrine and autonomic pathways that connect sleep with the immune system and the role of inflammatory peptides in the homeostatic regulation of**

**sleep.** Furthermore, I discuss the therapeutic potential of harnessing these reciprocal mechanisms of sleep–immune regulation to mitigate the risk of inflammatory and infectious diseases.

**And from the same paper…**
…partial night- time sleep deprivation activates inflammatory signalling pathways, such as those involving nuclear factor- κB (NF-κB), activator protein 1 (AP-1) and signal transducer and activator of transcription (STAT) family proteins, it increases levels of mRNAs encoding pro- inflammatory cytokines, and it increases TLR4 stimulated monocyte production of IL-6 and TNF.

…persistent sleep disturbance leads to sustained activation of the inflammatory response, which can be damaging to the host. In a meta- analysis of ~50,000 adults, **sleep disturbance was associated with higher levels of C-reactive protein (CRP) and IL-6,** with further evidence that increased levels of CRP occur even in individuals who have high variability in sleep duration between nights.

**…sleep promotes the activation of T cells through their increased production of IL-2 and IFNγ, as well as the production of IL-12 by dendritic cells and monocytes, which has a crucial role in inducing TH1 cell- type adaptive immune responses.**

**When sleep is experimentally disturbed, there is decreased production of IL-2 by T cells, a shift towards TH2 cell- type cytokine activity, decreased IL-12 production by monocytes and increased IL-10 expression. Similar alterations in the adaptive immune response profile are found in humans with chronic sleep disturbance.**

With regard to infection risk, short sleep duration predicts pneumonia risk (<5 hours sleep per night) and susceptibility to the common cold (<6 hours sleep per night). **In a retrospective study of ~23,000 adults, those who reported persistent short sleep duration (<5 hours per night) also reported an increased likelihood of cold or infection in the past 30 days.**