CONTENTS

# Physiology of Sleep

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“One of the misconceptions of sleep is that it’s a simple mechanism—it’s not,” says Ana Krieger, MD. “It’s a very complex cascade of several neurochemicals changing at the same time.”

A large majority of these complex cascades involve neurotransmitters, chemical messengers in the brain that promote or inhibit wakefulness. Chemicals that act as inhibitory neurotransmitters, such as GABA and adenosine, block the stimulating effect that keeps us awake, allowing the body to become sleepy. Research of adenosine suggests the chemical builds up in the body during wake hours, which causes drowsiness, and then degrades during sleep hours. Hence, caffeine stimulates the body by blocking adenosine receptors. Histamine, on the other hand, is a neurotransmitter that stimulates the brain, which is why antihistamines, such as Benadryl® and Tylenol PM®, cause drowsiness.

**Regulated Sleep**

Neurotransmitters also help regulate the sleep cycle, which is divided into five stages: REM and four phases of non-REM sleep that range from light sleep to deep sleep. Scientists have just begun to delve into why we need each stage of sleep, but what they do know is sleep is essential to a person’s health.

Most people spend about 20 percent of their sleep time in REM sleep, which is characterized by rapid eye movement and brain activity that most closely resembles that of being awake. Commonly thought to be involved in learning, memory, neuron repair and central nervous system development, REM is also the stage where dreams occur. Although the brain may be very active during REM sleep, neurotransmitters serotonin and norepinephrine inhibit muscle contraction, keeping the body immobile and preventing the person from acting out a dream while asleep. GABA is manipulated in several sleep medications because of its role in the pathway that controls non-REM sleep. Therefore, people taking GABA receptor-modulating drugs feel less rested than with natural sleep because they’re still not getting REM sleep.

During non-REM sleep, a person wakes up easier, maintains reflexes and has a regulated body temperature. Believed to be just as important as REM, non-REM

sleep is thought to be involved in growth hormone production and changes in the immune system.

**Circadian Rhythm**

Almost all living organisms possess an internal biological clock called a circadian rhythm. In humans, this clock signals the body when to wake, sleep and eat, but can be modified due to external stimulants, such as light.

Sensitivity to light, including its duration and brightness, by cells in the eye's retina produces a signal relaying this information to the suprachiasmatic nucleus, essentially the body's biological clock. This signal allows the release of melatonin from the pineal gland, increasing during the night and leveling off at dawn. The body uses these external cues to determine when to sleep and wake. In travelers with jet lag, the circadian rhythm is thrown off by the time difference in light stimulant, causing the body to readjust its internal clock over a couple of days.

**Sleep Research in Cancer**

In addition to the suprachiasmatic nucleus, researchers have also discovered that the liver and kidneys have circadian rhythms, as well as each individual cell in the body because of proteins and certain genes that regulate the body's internal clock. A gene identified in mice that regulates the circadian rhythm has been shown to affect a major tumor suppressor gene, possibly explaining studies that found night-shift workers are more likely to develop breast and colon cancer. Based on these findings, it's possible that their disrupted circadian rhythms may have affected regulation of cell division.

The circadian rhythm also regulates body temperature, blood pressure, stomach digestion and hormone secretion, and researchers are making use of this knowledge to treat patients. Chronotherapy looks at whether a patient's response to chemotherapy is different depending on the time of day and their natural circadian rhythm. The hope is that research will determine the best time of day for treatment for individual patients in regards to decreasing side effects and increasing anticancer activity.