Irregular Bedtimes and Awakenings

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KEYWORDS

• Irregular bedtimes • Awakenings • Circadian rhythm • Sleep disorders • Insomnia

KEY POINTS

- The body relies on a central pacemaker, the suprachiasmatic nucleus, to couple numerous physiologic patterns to the timing of light and darkness.
- Circadian rhythm disorders result when this synchrony is lost, including delayed sleep phase disorder, advanced sleep phase disorder, free-running disorder in the blind, and irregular sleep-wake disorder.
- A careful medical history with attention to symptoms of insomnia and excessive sleepiness, limited physical examination, and assessment of sleep timing with sleep logs and actigraphy may be informative.
- Treatments such as a regular sleep schedule, phototherapy, cognitive behavioral therapy for insomnia (CBTI), chronotherapy, and melatonin may be highly effective.

INTRODUCTION: NATURE OF THE PROBLEM

Like the rise and fall of the sun, sleep is presumed to be optimal when it follows a pattern of comparable regularity. Within an individual and across a population, however, there can be variability. Circadian rhythm disorders, in which patterns of wakefulness and sleep do not align with societal norms, may lead to significant problems. Lifestyle choices may also commonly affect the timing of sleep. Regardless of the cause, irregularity in the timing of sleep might compromise prompt sleep onset, introduce undesired awakenings, decrease sleep quantity and quality, and lead to important social consequences. To fully appreciate the importance of irregular sleep periods, it is necessary to have a basic understanding of the most common causes and the knowledge to evaluate and treat these disorders clinically.

Basics of Sleep and Circadian Rhythms

The propensity for sleep and wakefulness depends on 2 processes: homeostatic sleep drive and the circadian alerting system.[1] Sleep drive reflects the fact that the longer a person stays awake, the sleepier he or she will become, secondary to the buildup of chemicals within the brain that include adenosine.[2] With sleep, these natural hypnotic agents are cleared away and the desire for sleep subsides. To counteract the building sleepiness that occurs during prolonged wakefulness, the complementary circadian alerting system provides a gradually strengthened signal to stay awake.[3]

From the Latin meaning "about a day," the term circadian describes multiple endogenously generated physiologic processes that follow a nearly 24-hour pattern.[4] These processes include sleep propensity in addition to metabolism, core body

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temperature, cortisol levels, and plasma melatonin levels. These patterns rely on the interplay between elegant internal clock machinery and external time cues.

With the controls built into our genetic makeup, this machinery synchronizes rhythms that persist independently of exogenous influences. The first mammalian circadian gene, *Clock*, was identified in 1994.[5] Subsequently, multiple genes have been identified that constitute a core molecular clock that gives rise to a transcription and translation feedback loop of gene expression.[6] These genetic controls ultimately determine our body's overall circadian rhythmicity and, as a result, our risk of developing circadian rhythm disorders.

It is astounding to consider that every cell in our body follows a circadian pattern, a symphony of biochemical reactions that are perfectly timed based on available resources and orchestrated by a small group of cells in the anterior part of the brain's hypothalamus. This control center contains the master clock known as the suprachiasmatic nucleus (SCN).[7,8] Through hormonal and other as yet undetermined influences, the SCN coordinates the peripheral clocks that are present in cells as diverse as cardiac, liver, and adipose tissues.[9]

In constant conditions, the genetically determined period of biological rhythms, called tau, will be revealed.[10] It is typically more than 24 hours in length, but it may also be shorter. To realign this innate rhythmicity to synchronize with the actual geologic patterns of light and darkness, exogenous zeitgebers (from the German for "time givers") must be present.[4] This concept has important implications for the clinical treatment of the circadian rhythm sleep disorders.

Overview of the Circadian Rhythm Sleep Disorders

Disorders that are characterized by irregular bedtimes and awakenings are typically classified into several broad categories. The inability to fall or stay asleep may occur with insomnia, as discussed elsewhere. However, the most relevant disorders include those that directly affect the timing of the circadian rhythm.

How can the timing of sleep be disordered? This issue is ultimately one of perspective, influenced by social context. One must be careful in labeling normal variations of physiologic patterns such as sleep. When they lead to significant social and occupational dysfunction, however, it may be helpful to seek both diagnosis and treatment. Fortunately, for those whose irregular sleep patterns are without consequence, medical help is not typically sought.

In considering the circadian rhythm sleep disorders, it is important to understand not only the general characteristics but also the overall prevalence. These conditions are discussed in the remainder of this section and are summarized in **Box 1**.

Delayed sleep phase disorder

This condition is characterized by a delay in sleep onset and wake time by 3 to 6 hours relative to conventional sleep timing.[11] As a result, the patient will often initiate sleep between 2 and 6 AM and wake between 10 AM and 1 PM. Affected individuals often have sleep-onset insomnia, associated with increased alertness at night, and difficulty awakening at a socially acceptable time. It may be associated with prolonged hypnotic use and alcohol use at bedtime.[12] Caffeine and evening light exposure may exacerbate the condition. When sleep does occur, it is normal. It may result in impaired school and work performance, tardiness, absenteeism, and financial and relationship difficulties.

Delayed sleep phase disorder more often affects adolescents, but may persist throughout life. The prevalence among adolescents and young adults is estimated to be 7%.[13] It may drop to 0.7% among middle-aged adults.[14] Among patients presenting with complaints of insomnia to a sleep disorders clinic, up to 16% had the condition.[15] A positive family history exists in 40% of individuals.[16]

Advanced sleep phase disorder

At the other extreme, advanced sleep phase disorder is characterized by sleep and wake times that involuntarily occur 3 hours earlier than typical. Irresistible sleepiness may occur in the early evening, and early morning awakenings follow from 2 to 5 AM with complaints of insomnia. These awakenings occur even if bedtime is successfully delayed, often resulting in sleep deprivation. When sleep does occur, it is normal.[17]

The exact prevalence of advanced sleep phase disorder is unknown, but it is presumed to be rare and may not come to medical attention.[18] It is estimated to affect 1% of middle-aged adults and seems to increase with aging.[14]

Box 1
Circadian rhythm sleep disorders

Delayed sleep phase disorder

Advanced sleep phase disorder

Free-running disorder, or non–24-hour sleep-wake syndrome

Irregular sleep-wake disorder