

# Jet lag and other sleep disorders relevant to the traveler

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**Summary** Sleep and wakefulness are governed by homeostatic and circadian regulatory processes, and perturbations therein are primarily responsible for the sleep disturbances associated with travel. Misalignment between endogenous rhythms and the light/dark cycle can result in circadian rhythm sleep disorders, including jet lag. This condition will be the primary focus of this review, with an emphasis on predisposing factors, preventative options, and treatment strategies.

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## Overview of sleep disorders

During the past century, and particularly during the last several decades, there has been an unprecedented increase in understanding of sleep-related processes and pathology. Simultaneously, travel has become more commonplace, with the ability to traverse longer distances in shorter time periods than ever before. In this review, we will briefly discuss general sleep physiology, introduce a structure to understand sleep disorders and, finally, focus on those disorders that arise as a result of (or are influenced by) travel, with a particular emphasis on jet lag.

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## General sleep physiology

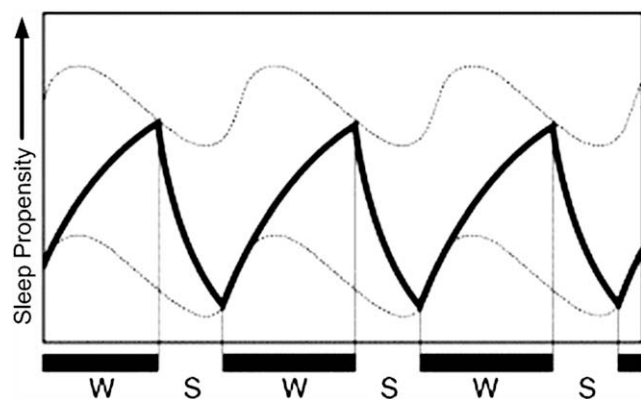
Sleep and wakefulness are conceptually governed by two processes, sleep homeostasis (process S) and circadian regulation (process C).<sup>1</sup> The homeostatic drive to sleep is proportional to the duration of wakefulness, and becomes maximal at about 40 h of complete sleep deprivation.<sup>2</sup> The nature of the biochemical substrate of process S is not yet certain, although several lines of evidence suggest that adenosine (which accumulates during extended wakefulness in the basal forebrain and returns toward baseline values after sleep recovery) may play a key role.<sup>3,4</sup> While process S therefore emanates solely from sleep/wake behaviors (and functions independently from the light–dark cycle), process C is dependent on rhythms intrinsic to the organism and creates a drive for wakefulness that variably opposes the homeostatic sleep drive (see Fig. 1). Master coordination of this sleep/wake rhythm (and

numerous other behavioral and physiological variables) is provided by the neurons of the suprachiasmatic nucleus, located within the hypothalamus.<sup>5–8</sup> Their rhythmic output results from an autoregulatory feedback loop in which oscillating circadian gene products regulate their own transcription and translation.<sup>49</sup> As this intrinsic period is typically slightly longer than 24 h,<sup>9</sup> synchronization to the 24-h day (entrainment) is accomplished by various environmental inputs (zeitgebers or “time givers”), the most important of which is photic exposure.<sup>10</sup>

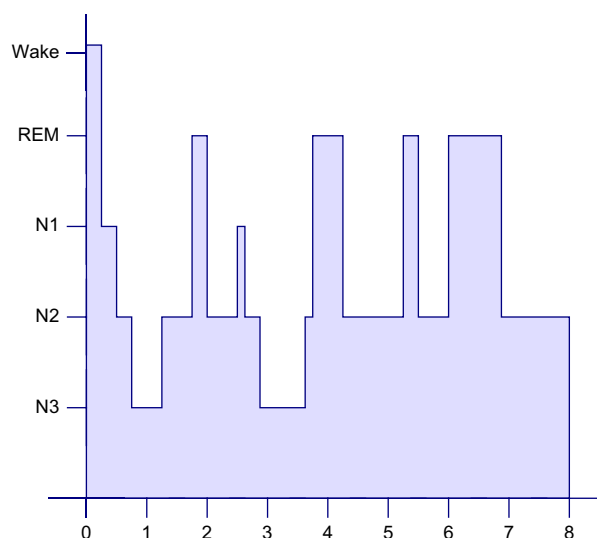
In addition to circadian and homeostatic processes, ultradian factors also influence physiologic variables during sleep.<sup>11</sup> Two main types of sleep have been differentiated based on electroencephalographic and electromyographic signals: rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. NREM sleep is further subdivided into three stages of progressive “depth” (N1–N3), with deeper stages requiring greater stimulation to arouse the sleeper. NREM and REM sleep cycle throughout the nocturnal sleep episode, with periods of REM appearing about every 90–120 min (Fig. 2).

## Sleep disorders

Disorders of sleep are predominantly classified into six categories: (1) insomnias, (2) sleep-related breathing disorders, (3) hypersomnias of central origin, (4) parasomnias, (5) sleep-related movement disorders, and (6) circadian rhythm sleep disorders (Table 1). Insomnia is characterized by difficulties with sleep initiation, maintenance, duration, or perceived quality, despite an adequate opportunity and environment for sleep, and with a concomitant daytime consequence or complaint. Sleep-related breathing disorders (such as sleep apnea syndromes) result from abnormal control or effectiveness of ventilation during sleep, and are among the most commonly diagnosed conditions within sleep clinics. The hypersomnias of central origin include those conditions that



**Figure 1** The two-process model of sleep regulation. Sleep propensity grows during wakeful periods (W) and abates during sleeping periods (S). Homeostatic process (process S – solid line) is limited to a certain range of values determined by a clock-like circadian process (process C – dotted lines) that varies with time of day. Modified with permission of publishers from Ref. 47.



**Figure 2** Normal hypnogram. Depicted is a stylized hypnogram showing the typical changes in sleep stage through one night of sleep. Stage N1 is a light stage, literally scored when the EEG shows features of sleep more than half the time, but without evidence of other stages of sleep. Stage N2 is the most prevalent, and is defined by characteristic EEG morphologies (K-complexes and spindles) in the absence of other sleep stage defining features. Stage N3 is “slow wave sleep,” and along with stage REM (rapid eye movement) is most demonstrably under homeostatic control. After acute sleep restriction, stage N3 debt is typically repaid first, with subsequent nights showing slightly extended REM to compensate for prior loss. Note the ultradian rhythm, where nearly every 2 h sleep alternates between non-REM and REM sleep.

are thought to originate from pathology within the central nervous system (e.g., narcolepsy). Parasomnias are disorders where complex undesirable activities, events, or experiences occur during or emanate from sleep (e.g., sleep walking, bruxism), and sleep-related movement disorders include neurological conditions that manifest during the sleep period (e.g., periodic limb movement disorder). Finally, circadian rhythm sleep disorders are conditions that arise from dyssynchrony between the light/dark cycle and the innate sleep/wake rhythm (e.g., jet lag), and are described in more detail below.

## General issues regarding sleep disorders and the traveler

The most common treatment interventions for patients with sleep disorders include cognitive-behavioral therapies, pharmacological treatments, and the use of breathing-assist devices, such as continuous positive airway pressure (CPAP) machines. Many sleep disorders are chronic conditions that require ongoing therapy, for which travel may impose certain inconveniences. For example, authorities may advise the traveler to keep prescription medications in the bottle, labeled with patient name, drug name, and prescriber. Although use of hypnotic drugs during long flights may be advantageous to enhance sleep and hasten adaptation to a new time zone, some may promote

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