The Sleep-Wake Cycle and Jet Lag

Trekking across time zones can disturb the body's natural rhythms, but melatonin may ease some effects of traveling.

By **W. STEVEN PRAY,** PH.D., R.PH., Professor of Nonprescription Products and Devices, School of Pharmacy, Southwestern Oklahoma State University, Weatherford, OK

Jet lag is one of many disorders of the sleep-wake cycle. One characteristic these daily rhythms, known as circadian rhythms, share is that they are partially controlled by one or more biological clocks.[1] Circadian rhythms recur in daily cycles roughly every 24 hours.

The circadian clock in mammals is centered in the hypothalamic region known as the suprachiasmatic nucleus. This hypothalamic regulatory center ensures that the mammal's behaviors and physiological responses are in harmony with the external environmental cycle of the sun. People generally function best when light and dark recur every 24 hours, allowing us to sleep, awaken, and eat at predictable times.

CIRCADIAN CYCLE

Researchers have performed isolation studies in which volunteers undergo long-term isolation from light-dark cues in the environment and from all other human contact. They eventually lose track of time in the real world, going to sleep and awakening whenever they feel the need. When people respond to their internal circadian clock, they create an artificial day for themselves that lasts 24.5–25.5 hours. Since each day consists of only 24 hours, this phenomenon answers the question of why people find it easy to stay awake an extra hour or two, but very difficult to go to sleep an hour or two earlier.

Our natural tendency to adapt to a 24.5- to 25.5-hour day helps explain the minor jet lag when a person flies three to four time zones to the east, where residents begin the sleep cycle 3–4 hours earlier than the traveler's time zone.[2] The Californian flying to New York enters a time zone that is three hours later, with bedtime at 11 pm, which is 8 pm in California.[3]

THE ROLE OF ZEITGEIBERS

Zeitgeiber is the term reserved for the external environmental clues we use to help us adapt to each day's 24-hour time progression. Zeitgeibers include the rising and setting of the sun, time of meals, activities of people around us, and various social activities. Individuals who have lost their vision often experience difficulty adapting to the constraints of the 24-hour daily cycle; this reinforces the importance of visual cues in establishing the internal clock.

BRIGHT LIGHT THERAPY

Bright light therapy may play a role in the treatment of jet lag. Bright light can actually shift the phase of the sleep-wake cycle in humans, which results in resetting of the circadian clock.[9] If the subject is exposed to bright light in the evening, melatonin secretion is delayed; if bright lights are suddenly turned on in the middle of the night, melatonin production immediately starts to drop. The hypothesized action of bright light is through direct suppression of pineal gland function. Light therapy is known to help such conditions as delayed sleep phase syndrome, seasonal affective disorder, and seasonally related bulimia. Though the use of bright light in jet lag is not well defined, some authorities suggest that if applied in the morning at the destination, it might depress endogenous melatonin secretion to more quickly regulate the person to the new sleep-wake cycle.[5]

Our bodies are conditioned to work in synchrony with the zeitgeibers of our home location. Body functions that undergo daily rhythmicity (e.g., hormone secretion, body temperature, intrinsic alertness) vary in a predictable manner as the day proceeds. The major factor causing jet lag is discoordination of the body's normal fluctuations with the normal daily progression due to a rapid shift in time zones.[4]

The human internal clock resets fairly slowly. If the person travels eastward, the internal clock resets at a rate of about one hour per day; adaptation to westbound travel occurs at a rate of about 90 minutes daily.

JET LAG

Of the millions of travelers who jet across time zones each year, as many as 80% report sleep disruptions.[1] Jet lag was first reported in 1931 by pioneering aviators Wiley Post and Harold Gatty after a transmeridian flight of 8 days and 16 hours.[5]

The most well-known sign of jet lag is a slowly declining sleep disturbance, occurring on the first night in 60%–70% of those who crossing a time zone, but only in 30% by the third night.[6] Other symptoms also have been attributed to jet lag: dyspepsia or constipation (perhaps a result of changing meal times), depression, disorientation, and lessened ability to estimate time, space and distance.[6]

Frequent fliers who suffer chronic sleep disruptions often develop malaise, irritability, and impaired performance on tasks requiring attention. In addition, menstrual cycles become irregular in females with recurrent jet lag.[6]

Some symptoms attributed to jet lag are actually due to being confined in an airplane. These include ophthalmic and nasal irritation, muscle cramps, nausea and abdominal distention, headache, edema in the legs and feet, and dizziness.[1] They usually disappear shortly after the flight is terminated.[1]

ROLE OF MELATONIN

The patient leaflet describes one possible intervention to prevent jet lag, preadaptation prior to departure.[7] However, much preliminary research has been conducted on potentially valuable treatments such as exercise, light therapy and melatonin to combat jet lag.

Melatonin is not yet approved by the FDA as safe and effective for any use. Nevertheless, people are using it and it is sold in many U.S. pharmacies. In Canada, it was pulled off the market a number of years ago, pending further research on safety and efficacy.

Melatonin is secreted by the pineal gland. A tryptamine derivative, melatonin is a chronobiotic medication, one of a group of active compounds capable of performing chronomodulation.[8] Melatonin secretion varies according to the season of the year. During the summer, when daylight is long and darkness is short, melatonin is secreted for only a short period. However, during winter, when daylight is short and darkness long, melatonin secretion is correspondingly longer.[9] In animals that live in regions with great seasonal changes, melatonin plays a large role in triggering seasonal behavior such as hibernation or breeding. Although seasonal secretion is also seen in humans, man is not a seasonal animal; any role in the human would rely mainly upon daily changes in melatonin secretion.[9] Melatonin secretion in humans is low during the first three months after birth, but increases. It peaks at ages 4–7 and then drops slowly.[10] The average amount produced by a male adult is 30 micrograms daily.[11] Each person's secretion pattern is unique and can be reliably reproduced day to day. Typically, melatonin secretion rises from a low basal level (perhaps 10 pg/mL) at about 10 pm, reaching a peak at 2–4 am (perhaps as high as

120–140 pg/mL) and declines to the basal level by about 8–9 am.[12] The morning decline occurs whether or not a person actually sleeps during the night. Individual differences in the times of the peak and trough may determine whether one is considered a "morning" or "evening" person.

Melatonin's sedative effect accounts for its use in insomnia (in a dose of perhaps 2 mg daily). It may be helpful in jet lag, in which the endogenous sleep cycle must change to correspond to the destination.[6] In one study, patients traveling east from San Francisco to London (eight time zones) experienced a decrease in jet lag when given 5 mg of melatonin daily starting three days prior to departure.[10] The dose was continued for four days after arrival.[12] In another study involving crossing of eight time zones, a 10 mg dose helped prevent sleep disruptions and cognitive impairment.[13] A peak blood level of melatonin is reached in perhaps one hour, with a rapid decline after 4 hours; sustained-release products may maintain blood levels 7 hours.[11] Pharmacists should not recommend melatonin for patients taking corticosteroids due to possible interactions.[11] Melatonin may prevent conception, and adversely affect pregnant or breast-feeding women.

DOES EXOGENOUS MELATONIN AFFECT ENDOGENOUS PINEAL SECRETION?

If long-term use of corticosteroids can affect the human feedback loop to down-regulate endogenous steroid production, can exogenous melatonin also produce this adverse effect? It may be that people taking continual doses of melatonin will experience rebound sleeplessness upon withdrawal. Until long-term use is proven safe, pharmacists should advise to limit melatonin use to a few days.

WHAT TO DO ABOUT JET LAG

Many years ago, there was no such thing as jet lag. When people wished to travel across the country, the trip took weeks in covered wagons or on horseback. Even in the early part of the 1900s, travel across several time zones may have taken longer than one week.

However, with the invention of high-speed jets, people began to notice that travel across time zones caused problems going to sleep or staying awake at the destination.

WHAT DETERMINES THE SEVERITY OF JET LAG?

How severe a person's jet lag is depends on several things. If you cross only one time zone, jet lag will probably not be noticeable. However, the more time zones you cross, the worse the potential problem. Crossing three or four time zones will probably cause trouble sleeping that lasts for only two to four nights before you adapt to the new time zone.

Imagine what jet lag can be like for the person who must cross six or more time zones. Consider the plight of a student from India studying in the United States who decides to travel home for the intersemester vacation. In this case, sleep disturbances may last as long as 10 days after arrival in India, and also may last as long as 10 days after returning to the United States.

DOES DIRECTION OF TRAVEL MAKE A DIFFERENCE?

One can predict what type of sleep disturbance will occur, depending on the direction of flight and the time at the destination. For instance, if a flight is from west to east, and if it crosses three time zones, as from California to Florida, the person arrives in a Florida time zone that is three hours later. If the person normally goes to bed at midnight in California and tries to go to bed at midnight in Florida, he or she will probably lie awake sleepless for several nights since midnight in Florida is 9 pm California time. Midnight in Florida is actually 9 pm according to this traveler's internal clock.

On the other hand, a New York native would experience the opposite problem on the West Coast. He would become sleepy at 9 pm, which would be midnight according to his New York internal clock.

HOW CAN JET LAG BE MINIMIZED?

If you will cross 2–4 time zones for a short period (no more than a few days), the simplest remedy is to keep mealtimes and sleep times the same as the home times. However, if the stay is longer, it is better to change one's schedule to match the destination times. For a few days before leaving the home time zone, try to stay up later or go to bed earlier, depending on the destination time zone. Immediately upon arrival, adopt the local schedule for mealtimes and bedtime. Avoid napping during the day at the destination since this delays the body's change to the new schedule. The jet lag diet publicized in the lay press in the 1980s is not helpful since it recommends the use of caffeine at bedtime.

Physicians may prescribe a medication to help deal with insomnia, but it should be stopped as soon as possible to allow the body to reset its internal clock naturally. Melatonin may reduce the symptoms of jet lag. ■

REFERENCES:

1. Wagner DR. Disorders of the circadian sleep-wake cycle. Neurol Clin. 1996;14:651-670.
2. Moline ML, Pollak CP, Monk TH, et al. Age-related differences in recovery from simulated jet lag. Sleep. 1992;15:28-40.
3. Steenland K, Deddens JA. Effect of travel and rest on performance of professional basketball players. Sleep. 1997;20:366-369.
4. Nicholson AN, Pascoe PA, Spencer MB, et al. Jet lag and motion sickness. Br Med Bull. 1993;49:285-304.
5. Wetterberg L. Light and biological rhythms. J Intern Med. 1994;235:5-19.
6. Manfredini R, Manfredini F, Fersini C, et al. Circadian rhythms, athletic performance, and jet lag. Br J Sports Med. 1998;32:101-106.
7. Sedgwick PM. Disorders of the sleep-wake cycle in adults. Postgrad Med J. 1998;74:134-138.
8. Shiota M, Sudou M, Ohshima M. Using outdoor exercise to decrease jet lag in airline crewmembers. Aviat Space Environ Med. 1996;67:1155-1160.
9. Brown GM. Light, melatonin and the sleep-wake cycle. J Psychiatry Neurosci. 1994;19:345-353.
10. Brown GM. Day-night rhythm disturbance, pineal function and human disease. Horm Res. 1992;37 Suppl 3:105-111.
11. Kendler BS. Melatonin: Media hype or therapeutic breakthrough? Nurse Pract 1997;22:66-67, 71-72, 77.
12. Croughs RJM, de Bruin TWA. Melatonin and jet lag. Neth Med J. 1996;49:164-166.
13. Comperatore CA, Lieberman HR, Kirby AW, et al. Melatonin efficacy in aviation missions requiring rapid deployment and night operations. Aviat Space Environ Med. 1996;67:520-524.