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# Tossing and Turning

BY ELIZABETH WHITTINGTON

*Treatment and side effects disrupt sleep.*

When Dawn McGovern, of Bunnell, Florida, started chemotherapy for leukemia, she couldn't sleep. Lying in bed at night, she would wake up frequently and ultimately move to the couch so as not to wake her husband.

For months, she continued the pattern of lightly dozing, waking up and eventually falling asleep around 7 in the morning. Even though her insomnia—probably a side effect of chemotherapy—has become a serious detriment to her quality of life, she has never considered it a high priority, including during her oncology visits.

“I might have mentioned to my doctor that I don't sleep well, but I didn't discuss it any further,” says McGovern, 43. But with maintenance chemotherapy on her calendar for another year and a half, McGovern says she will have to eventually talk at length with her oncologist about her sleep issues.



Dawn McGovern plans to talk to her doctor about options to help her sleep. Photo by Martha Goudey

A quarter of Americans report having a sleep disorder, but in the cancer population, the percentage jumps to nearly half as cited by the National Cancer Institute. And that number may be underrepresented since studies have reported as many as 90 percent of patients have some sort of sleep disturbance during and after treatment.

“Sleep complaints are major complaints of cancer patients but frequently unrecognized, and cancer doctors and other medical professionals don't ask about it,” says Dave Balachandran, MD, director of M.D. Anderson Cancer Center's new sleep center in Houston. Dr. Balachandran suggests patients open a discussion with their doctor by describing their specific sleep issues. The physician can then determine possible underlying causes and the best way to treat the sleep disorder, options that range from behavioral changes to medication.

[What Ails You?](#)

Insomnia is the most common sleep complaint of patients, but not getting quality sleep or waking up throughout the night can be just as detrimental. Other patients suffer from hypersomnia, or overwhelming daytime sleepiness, a condition different from fatigue, which is defined as the absence of energy. Sleep apnea, also frequently found in cancer patients, is when the patient stops breathing for several seconds throughout the night, either due to irregularities in brain signals or because the soft tissue in the back of the throat relaxes and blocks the air passage. While the person does not fully wake up, the body comes out of deep sleep to catch its breath, and the person wakes in the morning feeling as if they haven't slept well.

Pinpointing the cause of a patient's sleep disorder is necessary before treating it because symptoms of cancer and therapy side effects, such as coughing, pain, nausea and diarrhea, can restrict deep sleep. If the cause is treated, the sleep disorder will correct itself, but poor sleep hygiene can also be a culprit.

Recently, doctors noticed restless leg syndrome (RLS) is more common in cancer patients than previously thought. Anemia in patients can cause fatigue, but researchers now believe anemia may also contribute to RLS, especially for those with iron deficiencies or renal disease caused by chemotherapy. Research is also examining whether patients with head and neck cancer have more obstructive sleep apnea than other cancer patients, and if patients with brain tumors have problems with sleep because of altered brain function.

"We need to be more aware and address these issues—not just by giving a pill, but trying to understand what's causing sleep disruptions in patients," says Dr. Balachandran. "If certain cancer populations are more susceptible to sleep disorders, how can we best evaluate and treat them?"

## Behavioral Therapy

When M.D. Anderson recently examined its pharmacy prescriptions, Dr. Balachandran says Ambien® (zolpidem) was one of the most common non-chemotherapeutic drugs prescribed—a sign that when a sleep disorder is recognized, doctors may be too quick to prescribe medication despite studies and expert opinion that says the best initial approach is behavioral therapy.

A report in the *Journal of the American Medical Association* this past summer, showed that six weeks of behavioral therapy—which included improving sleep hygiene, cognitive therapy and relaxation—was more effective than a prescription sleep aid. After six months, patients with chronic insomnia in the behavioral therapy group spent less time awake and more time in deep sleep than patients who took medication.

"A lot of patients develop poor attitudes toward sleep because it's so frustrating getting to sleep," says Dr. Balachandran, who is helping patients reanalyze their feelings toward sleep using cognitive therapy—educating patients on their misconceptions of sleep to help correct the sleep disorder.

One cognitive therapy technique is finding a place other than the bedroom where the patient feels comfortable to sleep, such as a guest room, couch or hotel. "If they can sleep well in another environment, then it's not the patient, but the

association with the bedroom that interferes with sleep,” says Ana Krieger, MD, director of the New York University Sleep Disorders Center, who says up to 10 percent of her patients have cancer.

While undergoing therapy for stage 2 breast cancer, Deborah Copeland would awake at 11 each night. But instead of trying to go back to sleep, she would clean, watch television and keep herself busy until she was sleepy again in the early morning hours. During the day, she would take naps.

“I just accepted that this is the way it is,” says Copeland, a special education teacher from New York. When behaviors perpetuate sleep disorders, such as working on a project once awake, sleep clinicians say behavioral therapy can aid patients such as Copeland, who admits she feels tired during the day but enjoys the boosts of late-night energy.

Complementary therapy, such as acupuncture, imagery or even drinking warm milk, which contains tryptophan, an amino acid that is a natural sedative, may be helpful for some people. Studies have also shown exercise during the day, relaxation techniques and yoga can also help patients with insomnia get to sleep. A recent study showed a group of cancer patients who participated in a Tibetan yoga class had fewer sleep disturbances during follow-up when compared with patients who received standard care. The yoga group reported they slept better, went to sleep faster, stayed asleep longer and took fewer sleep medications.

“The study wasn’t specifically designed for sleep, although we do know that sleep problems are a common complaint,” says lead author Lorenzo Cohen, PhD, director of the integrative medicine program at M.D. Anderson. “But we did include a well-validated measure that tracks sleep disturbances because we thought it would be helpful.” A larger follow-up study of yoga in breast cancer patients undergoing chemotherapy is under way.

## Drug Therapy

“Many cancer patients have strong reservations about sleep medications, and if they believe that a drug is the only treatment option, a large segment of them may elect to continue enduring sleep difficulties rather than taking sleeping pills,” says sleep researcher Rami Sela, PhD, a professor of oncology at the University of Alberta in Canada. But when behavioral techniques do not work, sleep medications may be used for short-term relief.

“Depending on the stage of cancer, we can treat patients successfully and take away some of their frustrations by using medications,” says Dr. Krieger, especially if patients have had severe sleep problems for long periods of time. “Medication can take the edge off so patients can work on those behavioral techniques.”

A decade ago, patients had few drug options for treating sleep disorders. Doctors would prescribe benzodiazepines, such as Halcion® (triazolam) and Ativan® (lorazepam), which, although effective, are only prescribed for short-term relief because of the potential to become habit-forming and cause unwanted side effects, such as disorientation in the morning.

Newer sleep aids, including Ambien, Sonata® (zaleplon) and Lunesta®

(eszopiclone), have a much lower risk of becoming addictive and work slightly different than benzodiazepines. Whereas benzodiazepines bind to three different sites on a specific receptor for a chemical called GABA, these newer drugs selectively bind to only one of the receptor's sites, eliminating the side effects of binding to the other two. However, as reported in the journal *Sleep*, about half of patients, especially those over 65 or with public health insurance, are still prescribed the older class of sleep aids.

[View Illustration: Sleep Drugs at Work](#)

Non-benzodiazepines all work by enhancing the effect of GABA, which is an inhibitor neurotransmitter that induces sleep, but because each medication has a slightly different half life (the time the drug stays active in the body), patients should discuss their sleep issues with a doctor to determine the best medication. For instance, Ambien is not an immediate sleep aid and lasts for up to five hours. Typically, patients take Ambien at bedtime, but because it is quickly metabolized, the medication may lose its effect if a patient has a problem with waking up during the night. A new formulation of the drug, AmbienCR has extra medication in a time-release capsule that extends sleep throughout the night, but may cause a "sleep hangover" in the morning.

Sonata, on the other hand, only lasts for up to four hours, but acts within 15 minutes. Sonata may be appropriate for patients who wake up in the middle of the night and can't go back to sleep. And because of its short half-life, patients wake up in the morning with less grogginess than the longer-lasting medications. Lunesta, which is approved for long-term use, lasts longer than both Ambien and Sonata, but with any sleep medication, patients may not feel as rested as they would with natural sleep. "The insomnia may be cured, but medications don't necessarily guarantee restful sleep," says Dr. Krieger. Since sleep aids only increase non-REM sleep, the patient may still not achieve REM sleep, believed to be one of the most crucial sleep stages. Side effects of these drugs include possible dizziness, headache and aftertaste.

The newest competitor on the sleep market is Rozerem® (ramelteon), which has a different mechanism than the GABA receptor modulators. Rozerem mimics melatonin, a signaling hormone and one of the body's first signs that it should prepare for sleep. Believed to be necessary for the body's circadian rhythm, melatonin binds to its receptors in a central location in the hypothalamus called the suprachiasmatic nucleus, which signals that it is time for sleep.

Current data suggest sleep problems in breast cancer patients may be caused by abnormal circadian rhythms. "If research identifies that there are alterations in circadian rhythms in their sleep, we now have Rozerem," says Dr. Balachandran. "It can actually promote sleep in a more biological mechanism."

Approved by the Food and Drug Administration in July 2005, Rozerem is the first sleep aid to not carry a warning about possible addiction. Because of its different mechanism of action, Rozerem may not be the best medication for someone who needs sleep immediately because it takes time for the drug to begin working.

While these medications do work in some patients, experts say they need to be used in addition to a program with cognitive and behavioral therapy, and under close supervision. Most sleep-inducing drugs are not recommended for

long-term use, which is why it's important for a patient to be followed by a doctor and not just have a continually renewed pharmacy prescription.

“It is essential to help cancer patients who suffer from long-term insomnia realize that lasting improvement is likely to come from slowly developing new habits and skills relating to sleep. Within this context, sleep medication, though potent, is only one part of a comprehensive treatment program,” says Dr. Sela.

While research into sleep continues to unlock many of its secrets, such as uncovering the layers of sleep stages and the purpose of sleep, scientists are also looking into how sleep affects the immune system in cancer patients and when best to give chemotherapy in regards to patients' individual circadian rhythms. Currently, several ongoing clinical trials are examining sleep issues in cancer patients and how to best treat them, including trials with valerian, an herbal supplement, and the antidepressant Effexor® (venlafaxine).

McGovern, who continually suffers from fatigue and cognitive dysfunction, or chemobrain—which she surmises is partly attributed to her lack of sleep—says she may become interested in behavioral therapy or joining a clinical trial to solve her sleep problems if they persist. “I'll be on chemotherapy until May 2008,” she says. “That's a long time to not be able to sleep.”