Melatonin is the latest in a long series of "alternative" medicine "miracles." It has been described as useful for treating or preventing jet lag, insomnia, immune disorders, cancer and the degenerative effects of aging and for the enhancement of sexual function. A supposed benefit of this product is that it is "natural" in the sense that humans normally produce it in their bodies. Thus, people who avoid over-the-counter sleep aids can presumably relax about taking melatonin.

Unfortunately, like many other widely touted natural products, melatonin will not fulfill all its promoters' many promises. As it is sold over the counter today, melatonin is as likely to harm as to help.

Melatonin is a hormone produced from the amino acid tryptophan by the pineal gland, a small pinecone-shaped gland in the center of the brain. Melatonin production normally peaks around the time of puberty and then decreases with age. The most rapid decline usually occurs after age 40.

The production and secretion of melatonin increase tenfold in the dark and signal the body that it is time to sleep. This effect is well known and is the basis for the use of melatonin as a sleep aid. But melatonin has other effects that may lessen its usefulness. As with all drugs, while a little can be good, a lot can have negative effects.

In about 10 percent of the people followed thus far in studies of the hormone, high doses of melatonin have caused insomnia and nightmares rather than peaceful sleep. One high-dose study noted mental impairment in subjects, and subjects in another study reported severe headaches. Very high doses of melatonin have been found to affect other hormones: Estrogen, testosterone and thyroid hormone production are all decreased by high-dose melatonin. Melatonin also may affect the immune system. The hormone may be viewed as giving immunity a "boost"; but this is not necessarily a positive effect for some people, including those with immune disorders.

Although melatonin can affect some reproductive hormones, it has never been demonstrated to enhance sexual performance in humans. Indeed, Dr. William Regelson, coauthor of the book *The Melatonin Miracle* (Simon & Schuster, 1995), admitted in a recent television appearance that the claim that melatonin is a sex enhancer is simply a promotional claim, not a scientifically demonstrated fact.

**Unregulated Dose and Purity**
Richard Wurtman, a researcher at the Massachusetts Institute of Technology, has studied the effects of melatonin on sleep and has found the maximal effective sleep-inducing dose to be 0.1 to 0.3 milligrams (mg). Yet the most widely available over-the-counter dosage of melatonin is 2 to 3 mg in other words, up to 10 times the maximal effective dose (supplements in even larger amounts are also available).

Such large doses result in blood levels of melatonin that can be 30- to 50-fold higher than normal sleep levels, because blood levels increase exponentially rather than linearly with increasing oral dosage. This magnifies negative effects: At a 1 mg oral dose, excessive hypothermia starts. At doses above 1 mg, some workers have reported mental impairment and drowsiness the next morning because melatonin levels are still high at that time.

Another drawback to the use of the currently available melatonin is that there is no governmental authority ensuring its safety or purity. The passage of the so-called "Hatch amendment," the Dietary Supplement Health and Education Act of 1994, ensures that supplement manufacturers do not have to show that their products are safe, effective or pure before selling them to the public. We repeat: The Food and Drug Administration has no jurisdiction over the safety or effectiveness of these products unless and until they are shown to have caused harm. What this may mean is that with the current popularity of melatonin, we are seeing the stage set for a repeat of the tragedies that surrounded L-tryptophan supplements.

In the 1980s, the amino acid L-tryptophan was promoted as a "natural" sleep inducer, much as melatonin is promoted today. Unfortunately, a "glitch" developed in the manufacture of the L-tryptophan. In one or more large batches, instead of individual amino acid molecules being made, in many instances two L-tryptophans stuck together. This so-called "contaminant" was able to go wherever L-tryptophan went in the body; but instead of being used normally by the body's machinery, the double molecule jammed the machinery. Over 40 people died; and over 2,000 developed eosinophilia-myalgia syndrome (EMS), a disabling muscle disorder.

Lessons from Other Hormones and "Natural Products"

While the lack of enforceable standards of purity and safety is a real health threat to the consumer, it is important to note that the most common error people make in favoring "natural" supplements over "synthetic" drugs is the belief that if a substance is "natural," it's totally beneficial and mild it can't cause harm. There has been ample demonstration that this attitude is totally unrealistic not to mention the fact that most of the melatonin sold in stores is actually synthetic, not natural. In fact, all so-called "natural" supplements are manufactured using standard pharmaceutical techniques.

The melatonin sold in health-food stores may be either "natural" or synthetic. The "natural" form is extracted from the pineal glands of animals usually sheep. Pineal glands contain only minuscule amounts of melatonin, however, so it would take approximately 30 million sheep pineal glands to provide the melatonin found in one 100-count bottle of tablets, each tablet containing 3 mg of melatonin. Obviously, there aren't enough sheep on earth to supply all the so-called "natural" melatonin currently on health-food-store shelves! Thus, any so-called "natural" melatonin must include the synthetic form. Furthermore, without proper processing, viruses may contaminate animal-derived melatonin. For this reason, consumers who wish to use melatonin should use only
If we examine the use of hormones (such as melatonin) for "alternative" purposes, examples of harm abound. One example, of course, is the use of thyroid hormone as a weight-loss aid. Yes, thyroid hormone does speed up the body's metabolic machinery and help burn energy faster. When it is taken for long-enough periods and in large-enough doses, however, thyroid hormone causes heart damage and other ills.

Another example of hormone abuse is the use of anabolic steroids by bodybuilders who want to "bulk up" for a competition or by other athletes who want to increase their muscle mass and strength. Steroids can help do this, but their use exacts a price: only acne in some people, but mood changes, infertility and even death in others. Anabolic steroids taken orally offer a classic case of the short-term benefit and long-term harm that can result from taking additional hormones to supplement the ones we make ourselves.

Responsible medical practitioners are cautious about melatonin because there have been no studies of the safety of its long-term use in humans. We are ignorant about what might happen if a young man or woman were to begin using melatonin in his or her twenties and continue to use it regularly for the next 10 or 15 years or more. Would a long-term user become dependent on the hormone? Would his or her own natural production of melatonin be suppressed? Would a long-term user suffer permanent neuropsychiatric damage? And all this is aside from the problems that might arise from melatonin's depressing effect on reproductive and thyroid hormones: Dr. Regelson states in *The Melatonin Miracle* that 75 mg of melatonin acts as a contraceptive.

### Considerations for Use in Insomnia

The prudent consumer should be wary of the "natural" hype of the supplement manufacturers; the only well-substantiated effect melatonin has been shown to have is its effect as a sleep inducer at doses of 0.1 to 0.3 mg. Using the substance at the tenfold-higher-than-effective doses now found in health-food stores leaves the consumer open not only to possibly dangerous side effects but also to possible effects from unregulated and uncontrolled manufacturing processes. It may be difficult to find low doses, leaving current consumers with the option of dividing high-dose tablets or capsules into tenths not a very convenient procedure.

Anyone suffering from occasional insomnia who is interested in taking melatonin to deal with this condition should be sure:

* that the dosage is not above the effective level; i.e., 0.1-0.3 mg;
* that he or she takes it at the appropriate time; i.e., in the evening, about one half hour before going to bed;
* that he or she takes it under appropriate medical supervision.

Consumers should also be aware that sleep-promoting compounds are found in a number of foods. Rather than popping a pill at bedtime, a person with a mild case of sleeplessness could try a bedtime snack that included foods such as milk, peanuts, turkey, chicken or almonds. All of these foods contain tryptophan, which raises brain serotonin that in turn can be converted to melatonin.
Eating a tryptophan-containing food along with a high-carbohydrate food will help enhance the entry of tryptophan into the brain. Thus, Grandma's bedtime warm milk with honey is actually a sound sleep aid! Many foods also contain melatonin, but in such tiny amounts that someone would have to eat an enormous amount to get an effective dose (a snack of 72 bananas, for example, to get 0.3 mg of melatonin).

It must be emphasized that we in no way advise the use of melatonin for chronic insomnia; and we certainly do not advise its use for the other ills it allegedly cures or prevents from cancer to the degenerative effects of old age. There have been no long-term clinical studies showing that melatonin is either effective or safe for these purposes. Furthermore, because we lack such information, it is especially important that particular groups of people avoid using melatonin (see sidebar).

Finally, anyone who decides to use melatonin should first consult with a knowledgeable physician, especially if the person considering melatonin is also taking any other medications.

*A hormone is a chemical secreted by one part of the body that exerts its effect on another part. For example, the hormone insulin is secreted by the pancreas and causes muscles to take up and use glucose.*

**Victor Herbert, M.D., J.D.,** is a professor at Mt. Sinai School of Medicine and a scientific advisor to the American Council on Science and Health.

**Ruth Kava, Ph.D., R.D.,** is director of nutrition at the American Council on Science and Health.

**Who Should Avoid Melatonin?**

1. Women who are trying to conceive, are pregnant or are nursing a baby. Large doses of melatonin may prevent ovulation, and the hormone has not been tested for effects on the fetus during pregnancy. Melatonin can be found in breast milk; the effect of large doses on nursing babies is unknown.
2. People with disorders involving the immune system, such as severe allergies, autoimmune diseases (like rheumatoid arthritis) or immune-system cancers (like lymphoma). High doses of melatonin may stimulate the immune system and may worsen such conditions.
3. Children, who naturally produce high levels of melatonin, should not take supplements of the hormone. Its effects on them are unknown.
4. People with severe mental illness. High doses given during the daytime have worsened the symptoms of some patients.
5. People taking steroid medications. Melatonin may counteract the drugs' therapeutic effects.
6. People under 40 years old. Normal melatonin production declines most rapidly only after age 40.
7. People taking monoamine oxidase (MAO) inhibitors. Current melatonin preparations may be contaminated by vasoactive amines.
8. People who don't want to lower their natural production of estrogen, testosterone and thyroid hormones, which high doses of melatonin will do.
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