

Melatonin Isn't Just for Sleeping – From Cardiovascular Disease and Cancer to Aging and Macular Degeneration the Research Will Shock You

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Hormones become deficient as our bodies get older. And these deficiencies are one of the root causes of all of the diseases and symptoms of aging. So, treating these deficiencies along with a healthy lifestyle is fundamental to living long and well. But of all the hormones that our bodies depend on, there is one particular hormone that stands out above all the others.

The surprising thing is that almost nobody fully appreciates how important this hormone is. I'm talking about melatonin. And when you hear about all of the things that researchers are discovering about melatonin, you're going to be absolutely amazed.

Everybody knows that melatonin is important for sleep. But it's my opinion that even if you sleep like a baby, if you are over the age of 40, you should be taking melatonin. This information is too significant to quickly gloss over. So, in this article I'm going to present you with 19 recent research papers that will tell you why it is so important that we all supplement with this very special hormone no matter how well we sleep. Specifically, I am going to show how this one hormone promotes all of these unexpected effects:

- Protects against viral and bacterial infections,

- Prevents cardiovascular disease and high blood pressure,
- Reduces oxidant stress and inflammation and slows aging,
- Prevents neurodegenerative diseases such as Parkinson's and Alzheimer's,
- Improves menopause therapy,
- Protects against ionizing radiation,
- Prevents macular degeneration, and
- Prevents and treats cancer.

First of all, some people may have a hard time understanding how melatonin can be so important for so many different aspects of the body. After all, isn't it produced only in the brain? That is one of the first misunderstandings that needs to be cleared up. No, melatonin is not produced only in the brain. It is produced all over the body in larger amounts than it's produced in the brain. The largest production of melatonin is in the intestines. Researchers have also discovered that it's produced in the retina, the bone marrow, the skin, the thymus, and the white cells of the immune system. The fact that it's made in the thymus, which is an important regulator of the immune system, and in the immune cells themselves is why melatonin is so important for preventing and treating infections and cancer.

Infections

Let me just quote for you from a recent review of the infection-fighting potential of melatonin. "Melatonin has also been found to be effective in combating various bacterial and viral infections. Its administration has been shown to be effective in controlling chlamydial infections, infections induced by *Mycobacterium tuberculosis*, and also in many viral infections."¹ The researchers go on to explain that melatonin is such an efficient anti-infectious supplement for several reasons.

For one, it can directly decrease bacteria's ability to reproduce. If bacteria cannot reproduce, they cannot infect. Secondly, it sets up an environment in our tissues that bacteria cannot survive in. And third, it acts to decrease the inflammatory effects of bacterial infections. This is why it's so effective in animal models of septic (infectious) shock.

Amazingly, the authors go on to say, "Use of melatonin has been beneficial in treating premature infants suffering from severe respiratory distress syndrome and septic shock." And, "It has a potential therapeutic value in treating septic shock and associated multi-organ failure in critically ill patients in addition to its antimicrobial and antiviral actions."

One of the real battles we have these days is the constant exposure to new viruses and antibiotic-resistant bacteria. Along with ozone therapy, melatonin could be just the answer we need. Both of these therapies not only strengthen our immune systems, but also have a direct effect on these infections.² I am sure that the reason we hear of old people dying from flu infections every year is because they are deficient in melatonin.

Cardiovascular Disease

Another effect of melatonin is in preventing and treating heart disease and high blood pressure. A brand-new review article on the effects of melatonin on cardiovascular disease points out that "the major contributor for morbidity and mortality of the impaired cardiovascular system" is not cholesterol or stress. It's getting older! The risks for coronary disease, high blood pressure, heart failure, and stroke increase with age more than any other risk factor. Why? The authors state that one of the reasons is because as we get older, our levels of melatonin decline to almost nothing. These researchers produced a number of remarkable studies on senescence-accelerated mice to make their point.

Senescence-accelerated mice are a special breed of mice that age much faster than regular mice. Compared to normal mice, these senescence-accelerated mice have much more inflammation and oxidative stress and die earlier. They also have much lower amounts of nitric oxide. Nitric oxide is critical for cardiovascular health and maintaining a healthy blood pressure.

So, the researchers gave the senescence-accelerated mice melatonin. They discovered, "Melatonin treatment prevented the age-dependent cardiac alterations observed in the senescence-accelerated prone group." In fact, when they were taking melatonin, the senescence-accelerated mice had the same level of cardiac function as normal mice!³ Why did they get these results? Because, as you will see in a moment, melatonin has remarkable anti-inflammatory and antioxidant properties. So, mice do

better with melatonin, but what about people?

Researchers recently looked at 16 men with high blood pressure. First, they measured their blood pressures using a 24-hour blood-pressure monitoring device. Then they gave each of the men a placebo pill to take before bed every night and re-measured their blood pressures. Then they repeated the experiment, but the second time they gave the men 2.5 mg of melatonin.

Another characteristic of melatonin is that it acts directly on the DNA and mitochondria in our cells, causing them to behave more like they did when we were younger.

They only did this for three weeks. But even in that short a period of time and with that low a dose, their systolic blood pressures dropped an average of six points, and the diastolic dropped an average of four points.⁴

Aging, Inflammation, Oxidant Stress

So, melatonin is protective for infections and cardiovascular disease. But what about aging and the diseases of aging? Everybody agrees that the two major causes of degenerative disease and the aging process are oxidant stress and inflammation. So, does melatonin have an effect on these?

A recent article on melatonin, aging, and the nervous system looked at the effect of melatonin on NF-kB. NF-kB is the protein complex that causes inflammation. One of the ways that NF-kB causes inflammation is by stimulating the pro-inflammatory enzyme COX-2. COX-2 is the enzyme that many of the anti-inflammatory drugs interfere with. These researchers found out that not only does melatonin inhibit NF-kB, it also suppresses COX-2. So, melatonin does have a strong anti-inflammatory action. By the way, another effect of the COX-2 enzyme is that it stimulates tumor development.⁵ Remember this when I discuss the role of melatonin to prevent and treat cancer. But that's not all.

Through many of the same mechanisms in which melatonin prevents inflammation it also stimulates Nrf2. Nrf2 is the main transcription

factor that stimulates the production of all of the antioxidant enzymes that the body uses to control oxidant stress. One of the reasons that ozone therapy is so effective for so many age-related diseases is because it is a potent Nrf2 stimulator. Nrf2 levels are directly related to how long you will live and what your risks are of becoming sick from anything. By decreasing inflammation and oxidant stress through the suppression of COX-

2 and of NFkB and the stimulation Nrf2, melatonin may be the most effective anti-aging supplement you can take.

Another characteristic of melatonin is that it acts directly on the DNA and mitochondria in our cells, causing them to behave more like they did when we were younger. Studies have shown that aging rats supplemented with melatonin are healthier and live 20% longer than their deficient friends. That's why researchers at the Menopause Center in the Madonna delle Grazie Health Institute in Rome decided that the way melatonin functions in the body of women as they near menopause might provide some clues for the aging process in both men and women.

They set up a double blinded, placebo-controlled study in a group of peri and post-menopausal women between the ages of 45 to 60. First, they measured their thyroid hormones, T4 and T3, and their melatonin levels. The researchers knew that as we get older our levels of thyroid hormones decrease. This leads not only to increased weight gain and decreased energy levels, but it also results in high cholesterol and a shorter life span. All of these symptoms are very common in the over-fifty crowd. Then they gave half of the women 3 mg of melatonin, and the other half a placebo. Three and six months later the same tests were repeated. Here's what they found out. Every single one of the women who had lowered levels of melatonin at

➤

Melatonin

➤ the beginning of the study showed a significant increase in the levels of both thyroid hormones.

According to the authors, "These findings seem to show a recovery of pituitary and thyroid functions in melatonin-treated women, towards a more youthful pattern of regulation."⁶

Anti-infectious, preventing cardiovascular disease, and anti-aging – so far so good. But what else? How about brain function?

Alzheimer's and Neurodegenerative Diseases

The data on melatonin and brain and nervous system function is astounding. Many of the problems that we face as we get older are directly related to nervous system aging. This includes declines in cognition and memory, impairments in vision and hearing, chronic constipation and other stomach and intestinal tract problems, decreased coordination, decreased balance, and falls. Studies say melatonin is effective for all of these problems.

In one recent study, the researchers looked at the levels of 6-sulfatoxymelatonin in the urine of 1,105 men and women between the ages of 64-78. This is a metabolite of melatonin that shows up in the urine. The more 6-sulfatoxymelatonin in your urine, the higher your levels of melatonin are. Then they measured their MMSE scores. The MMSE test is an easy to do test that I use in the office all the time to measure and monitor memory and cognitive function.

The men and women with the higher levels of 6-sulfatoxymelatonin and hence had the highest levels of melatonin also had the highest scores on the test. The researchers concluded that the higher your melatonin levels are, the less likely you are to have any kind of cognitive impairment.⁷ But why? What's going on?

First of all, melatonin is by far the major antioxidant in the brain and nervous system. Since oxidant stress is the primary destructive force on our brain's cells, having enough melatonin

is absolutely vital for preserving optimal brain function in the over-60 crew. Animal studies clearly show that melatonin protects brain cells as we get older more effectively than any other antioxidant supplement.

Here's a powerful example of how effective melatonin is at protecting the brain. Methamphetamine is a street drug that destroys brain cells. When researchers give animals melatonin supplements along with high doses of methamphetamine, they are completely protected from the damaging effects of the drug. But melatonin does much more than just protect the cells from degeneration. It also acts to stimulate brain stem-cell activity.⁸

You might not know this, but unlike all the other cells in the body, many brain cells do not divide and replace themselves before they die. You have these cells when you are young. But since they do not breed new daughter cells, when they die, they are gone for good. Don't worry, though. That's because we have brain stem cells. Brain stem cells are special cells that can magically turn into any one of the many cells that the brain has. So, when our non-multiplying brain cells die, our brain stem cells can come along and replace them. The process is called neurogenesis. That's great news, right? Not so fast.

Stem cells are amazing, but their activity decreases as we get older. As that happens, neurogenesis decreases. And that's another reason melatonin levels are so important. Because studies show that when researchers give animals melatonin supplements as they age, the process of neurogenesis goes the other way – it actually increases! But animals aren't the only ones who benefit.

In humans, scientists have found that giving melatonin supplements "potentiates hippocampal neurogenesis in elderly populations." Why is this so important? The hippocampus is the area in the brain that regulates short-term memory and spatial orientation. Spatial orientation refers to knowing where you are and how to get to where you want to go. In Alzheimer's disease, the hippocampus is one of the first regions

of the brain to suffer damage. And that's why memory loss and disorientation are two of the early symptoms.

A recent study looked at 80 men and women with mild to moderate Alzheimer's disease. The researchers gave half of them 3 mg of melatonin every night for four months. The other half got the placebo pill. According to the authors, "Melatonin treatment resulted in significant and clinically meaningful effects versus the placebo in mean IADL and MMSE scores."⁹ IADL refers to activities of daily living and scores how well patients are able to get around and take care of their basic needs. The MMSE I mentioned above. If melatonin can have this effect on patients with such a severe disorder as Alzheimer's, imagine what it can do for those without the disease.

Another study looked at the effect of taking melatonin to prevent Parkinson's disease. The researchers gave a group of mice the drug MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). This drug selectively destroys the dopaminergic cells in an area in the brain called the substantia nigra and causes Parkinson's disease. When the mice were pretreated with melatonin before being exposed to the drug, their brain cells were protected, and none of them developed the disease.¹⁰

Menopause

Melatonin is also important for women going through menopause. Just this past year researchers looked at the effects of melatonin on 240 menopausal women between the ages of 40-60 years. They divided the group in half and gave half of the women 3 mg of melatonin every night. The other half got the placebo. After three months the symptom scores in the melatonin group were cut in half. As expected, the symptoms in the placebo group did not change.¹¹

In the study I mentioned above from the Menopause Center in the Madonna delle Grazie Health Institute in Rome, the researchers also measured the luteinizing hormone and follicle stimulating hormone levels in the group of peri- and post-menopausal women. Luteinizing hormone and follicle

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stimulating hormone are pituitary hormones that regulate a woman's production of the ovarian hormones. Here's what they found.

The women with the lowest levels of melatonin had the highest levels of both luteinizing hormone and follicle stimulating hormone. This finding indicates that lower levels of melatonin are likely a trigger for menopause, since elevated levels of luteinizing hormone and follicle stimulating hormone are what happens to women as they enter menopause. This conclusion is further strengthened by the fact that within six months of receiving the 3 mg melatonin supplement, the younger women (43-49) showed a decrease in their levels of luteinizing hormone and follicle stimulating hormone to levels more typical of younger women. In addition, most of the melatonin-treated women reported a general improvement of mood and a significant decrease in symptoms of depression. Here's why this is important.

I see a lot of women for hormone replacement. Many of them come to see me because their doctors have been unable to effectively rid them of their menopausal symptoms using the customary combinations of bio-identical hormones. And I have learned over the years that what often makes the difference for these women is melatonin. So, whenever I am working to balance the hormones in either a peri- or post-menopausal women I always make sure to prescribe melatonin. It makes both of our lives a lot easier!

Ionizing Radiation

Here is an especially important role for melatonin. It has to do with ionizing radiation. Ionizing radiation causes cancer. Children are especially at risk. One of the most potent sources of ionizing radiation is doctors – specifically the x-rays we order. And x-rays are only a minor source of ionizing radiation compared to CT and PET scans. Just one CT scan exposes you to the same amount of ionizing radiation as 70 chest x-rays. And a combined CT/PET scan has almost two times the amount of radiation as a plain CT. And it is not uncommon for me to see patients getting 2-4 CT/PET scans

a year. That is an incredibly high amount of radiation and is sure to be unsafe. But not to worry. There is a simple, natural substance that you can get that can cancel the potentially damaging effects of ionizing radiation.

Researchers took blood samples from several men and women. Then they gave them a single dose of 300 mg of melatonin. One and two hours later they collected a second and third blood

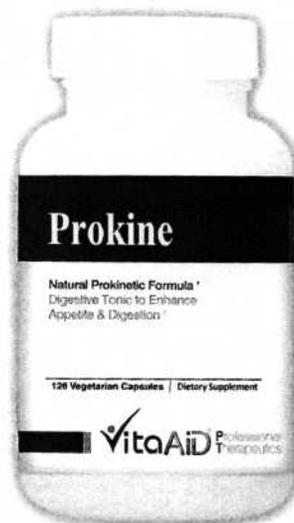
specimen. Then they exposed all of the blood specimens to a whopping dose of radiation (150 Gy) that was roughly the equivalent of 1000 CT scans. After the blood was irradiated, they tested the white blood cells to determine the extent of radiation-induced genetic damage.¹² Here's what they found.

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Melatonin

➤ The lymphocytes in all of the blood samples had a degree of genetic damage from the radiation. But the cells that were taken an hour after the melatonin dosing had significantly less genetic damage. And the ones taken at the two-hour mark had the least damage. The authors concluded that the data had important implications for the protection of our immune cells from the genetic damage induced by ionizing radiation. So, what does this mean for you? It means that if you are ever told that you need a CT scan or CT/PET scan, be sure to take 300 mg of melatonin about two hours before the procedure. You will basically eliminate any negative effects of the ionizing radiation.

Macular Degeneration

Several animal experiments have shown that melatonin protects against macular degeneration. This should not be too surprising for several reasons. One, studies have shown the both blood levels of melatonin and urine levels of 6-sulphatoxymelatonin, the metabolic breakdown product of melatonin are lower in people with macular degeneration than they are in people with healthy eyes. Two, melatonin is produced in the retina, the part of the eye that is affected by macular degeneration. Three, melatonin is the most powerful anti-oxidant in the eyes. And four, oxidative stress is the primary cause of macular degeneration.

One study looked at the effect of melatonin supplementation on rats that have been bred to develop macular degeneration. The researchers gave the animals a dose of melatonin that was equivalent to a 3 mg dose for humans. When they examined the eyes of the animals, they discovered that the melatonin decreased the incidence and severity of the damage to the retina, improved microscopic abnormalities associated with macular degeneration, prevented the structural and functional changes in retinal cells associated with macular degeneration, reduced the severity of microcirculatory disorders in the retina, and prevented

the destruction of neurosensory cells, associative and ganglionic neurons in the retina. According to the authors, "Taken together, our data suggest the therapeutic potential of Melatonin for treatment and prevention of macular degeneration."¹³

Another study reported on the effect of a melatonin supplement in 55 patients with either dry or wet macular degeneration. The natural history of macular degeneration is that it gets worse over time. But in this study, the melatonin supplement stopped the progression of the disease.¹⁴

Cancer

The last thing I want to share with you about melatonin is truly remarkable. Who would have guessed? Melatonin is one of the best supplements you could ever take for cancer. I treat a lot of patients with cancer. I believe one of the most important things I can give them is melatonin. Here's why.

Researchers looked at all of the controlled studies published on the use of melatonin in patients with cancer from 1993 to 2004. They were specifically looking at the rates of survival during the first year of treatment. They included trials that used melatonin as either the only treatment given or when it was given along with other treatments such as chemotherapy or radiation. The results were astounding.

The researchers reported that melatonin not only has been shown to have a direct anticancer action, but it also activates the body's immune reaction against cancer. Additionally, melatonin has been found to protect healthy cells from the negative effects of chemotherapy and radiation. All of this from a safe, inexpensive, natural substance. The authors also mentioned that there were no significant side effects reported in any of the studies. And here's the best news.

On average melatonin reduced the risk of dying by 44%! That's astounding. If results one-tenth this good happened from the use of a \$20,000 per month drug, Big Pharma would be touting it as the next great thing. But that's not all. The effects were consistent no matter

what dose they used. And none of the patients had any significant side effects from the melatonin. The authors put it this way, "The substantial reduction in risk of death, low adverse events reported, and low costs related to this intervention suggest great potential for melatonin in treating cancer."¹⁵

Despite incredible data like this, oncologists continue to be suspicious of using a natural substance along with their chemo or radiation. For reasons that always prove to be false, they keep suggesting that natural substances will somehow interfere with these therapies. That's why a brand-new animal study is so important.

The researchers took a group of rats who had estrogen positive breast cancer and divided them into four groups. One group received no treatment at all. They gave the second group melatonin. The third group got a chemo drug called adriamycin. And they gave the fourth group a combination of adriamycin and melatonin. Then they measured the amount of tumor growth, the microscopic changes in the tumors, and the survival rate of the animals after one month. Once again, the results are incredible.

Did the melatonin interfere with the chemo drug? Absolutely not. In fact, the tumors were smaller, and the amount of microscopic tumor cell injury was higher in the group that had the combination of melatonin and chemo than they were in the chemo-only group. Melatonin not only did not interfere with the drug, it actually improved the results. This is what I see 100% of the time when I combine natural therapies with conventional therapy for cancer.

But that's not all the researchers found. The group that had the highest one-month survival was the group that got the melatonin all by itself. And the one that had the most side effects and were the sickest was the one that had the drug by itself. The researchers concluded that adding melatonin to chemotherapy enhanced the treatment effect of the drug while at the same time decreased the side effects. But why?

In their words, it's because, "Melatonin has been shown to play a fundamental part in neuro-

immunomodulation." This means that it improves the way the immune system is able to kill the tumor. This is critical because chemo agents are immune suppressive drugs. Melatonin seems to protect the immune system from this effect. They also found that melatonin has its own direct action on tumor cells that kills them just like chemo does. Once again, in their own words, "A number of studies have documented that when given in combination with chemotherapy to patients with disseminated disease [stage 3 and 4 cancer], melatonin increases the overall one-year survival and reduces toxic side effects."¹⁶

One of the most important things that this study points out is that melatonin works well when it is used in combination with chemotherapy. According to another paper, "Because of its SERM (selective estrogen receptor modulators) and SEEM (selective estrogen enzyme modulators) properties, and its virtual absence of contraindications, melatonin could be an excellent adjuvant with the drugs currently used for breast cancer prevention (antiestrogens and antiaromatases). The antioxidant actions also make melatonin a suitable treatment to reduce oxidative stress associated with chemotherapy, especially with anthracyclines, and radiotherapy."¹⁷

If you are fighting cancer, or if you know anybody who is fighting it, this information is critical. It is critical for two reasons. One, as you have seen melatonin therapy will not only extend your life, but it will also improve the quality of your life. And two, although the information has been out for over 17 years you will still not hear it from any oncologist including the ones at the supposed great cancer centers. The next study was published in the *European Journal of Cancer* way back in 1999.¹⁸

The authors begin their report by stating that the hormone melatonin "...has been proven to counteract chemotherapy toxicity, by acting as an anti-oxidant agent, and to promote apoptosis of cancer cells, so enhancing chemotherapy cytotoxicity." Just to be clear, what they are saying here is

that melatonin decreases the toxicity of chemotherapy while at the same time increasing its ability to kill cancer cells. If that doesn't sound like the most perfect natural addition to conventional chemotherapy, then I don't know what does. So, based on this fact, the researchers set out to evaluate the effects of giving melatonin along with chemotherapy in several different cancers.

The researchers looked at a total of 250 men and women who had advanced, metastatic cancer: 104 had lung cancer, 77 had breast cancer, 42 had gastrointestinal tract cancer, and 27 had head and neck cancers. They gave some of the patients in each group 20 mg per day of melatonin in addition to their regular chemotherapy. The rest did not get the melatonin supplement. The following chemotherapy drugs were used: cisplatin, etoposide, gemcitabine, doxorubicin, mitoxantrone, paclitaxel, and 5-FU. Here's what happened.

According to the authors, "The 1-year survival rate and the objective tumor

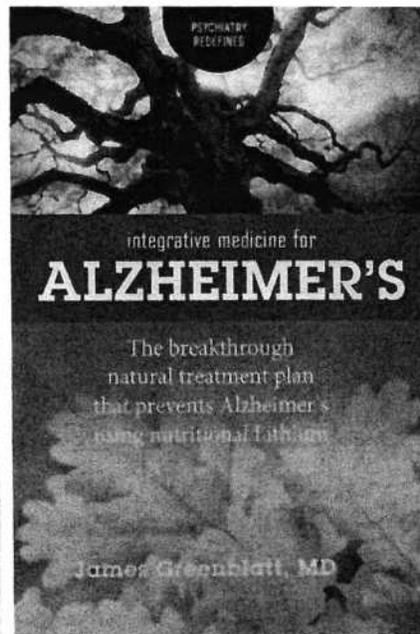
Melatonin

regression rate were significantly higher in patients concomitantly treated with melatonin than in those who received chemotherapy alone." Specifically, the chemotherapy was effective in killing the tumors in 34% of the patients taking the melatonin compared to only 15% in the non-melatonin group. That's more than a 100% improvement over chemo alone! Clearly, the melatonin dramatically improved the efficiency of the chemo drugs. And that's not all.

In terms of survival, the melatonin group had a 51% survival rate after one year compared to a 23% survival rate for the patients not getting the melatonin. The results mean that if you take melatonin along with your chemotherapy your treatments will be more than twice as effective, and you will be more than twice as likely to be alive a year later. Dear readers, if there was any drug out there right



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Melatonin

➤ now that was anywhere close to being this effective it would be all over the news, and every oncologist would be prescribing it. And once again, that's not all.

The melatonin also reduced side effects and improved the quality of life. Listen to the researchers once again:

Moreover, the concomitant administration of melatonin significantly reduced the frequency of thrombocytopenia [platelet destruction], neurotoxicity [nerve damage], cardiotoxicity [heart damage], stomatitis [mouth sores], and asthenia [weakness and poor appetite]. This study indicates that the pineal hormone melatonin may enhance the efficacy of chemotherapy and reduce its toxicity, at least in advanced cancer patients of poor clinical status.

Researchers in the Department of Cellular and Structural Biology, at the University of Texas Health Science Center in San Antonio studied the effects of the hormone melatonin on prostate cancer cells. They used two different cell lines. One was the LnCaP cells, and the other the PC3 cells. Both of these cell lines are human prostate cancer cells. The LnCaP cells are prostate cancer cells that are hormone sensitive. That means that their growth is stimulated by the hormone testosterone. The PC3 cells are not hormone sensitive. What they found should make us older guys sleep a little better.

The study looked at what happened to the growth rate of both kinds of cells when they were exposed to varying doses of melatonin. According to the researchers, "Melatonin treatment dramatically reduced the number of prostate cancer cells and stopped cell cycle progression in both LNCaP and PC3 cells." That means that no matter whether the prostate cancer cells were sensitive to testosterone or not, they were all stopped with melatonin.¹⁹

One study, entitled, "Melatonin in the treatment of cancer: a systematic review of randomized controlled trials and meta-analysis" summarizes the

known anti-cancer effects of melatonin. The researchers stated that, "Melatonin has oncostatic [anti-cancer] properties in a wide variety of tumors."¹⁵ This includes colorectal, breast, prostate, pancreas, liver, and brain cancer. It is particularly effective in estrogen receptor positive breast cancer because it regulates estrogen receptor expression and transactivation, and modulates the enzymes involved in the synthesis of estrogen. Melatonin also stimulates apoptosis.

Apoptosis is the mechanism that causes healthy cells to eventually die. It is how the body maintains a normal, healthy growth rate. The reason cancers are so lethal is because they find ways to avoid apoptosis. That allows them to continue to grow and spread without any restraint. As I mentioned above, melatonin activates the process of apoptosis in cancer cells, and thus limits the malignancy potential of cancer cells. Keep this in mind. The only problem with cancers is that they don't stop growing and spreading. If you have a cancer in your body that for some reason is not growing in size or spreading, it will never be a problem for you. I am convinced that many of you who have an as yet undiscovered cancer right now while reading this report can prevent that cancer from ever being a problem for you simply by taking a melatonin supplement.

Telomerase is another reason cancer cells don't stop growing and multiplying. Telomerase is an enzyme that can cause a cell to live way beyond its normal life expectancy. Unlike healthy cells, cancer cells can activate this enzyme, and just like with decreased apoptosis, activated telomerase can result in unrestricted cancer growth. That's the bad news. The good news is that melatonin inhibits telomerase activity in cancer cells. But increasing apoptosis and decreasing telomerase activity are not the only ways that melatonin stunts cancer growth.

Melatonin also inhibits angiogenesis. Angiogenesis is the mechanism that cancers use to grow new blood vessels. They use the newly developed blood vessels to increase the delivery of the sugar and other nutrients they need

to grow. The result is that they grow faster. There are drugs that oncologists use to decrease angiogenesis, but these drugs are so strong that they can create problems by inhibiting angiogenesis not only in cancers but also in healthy tissues. Unlike these drugs, melatonin is selective. It does not affect angiogenesis in healthy tissues.

Summation

Collectively, all of these effects – direct anticancer action, enhanced immune reaction against cancer, preventing the negative side effects of chemotherapy and radiation, apoptosis stimulation, telomerase inhibition, and angiogenesis inhibition – help to explain why melatonin should always be prescribed to both prevent cancer and as part of the overall treatment of cancer.

Melatonin Facts

Melatonin is produced and released in the pineal gland in the brain in darkness while you are sleeping. The release of all this wonderful melatonin is immediately suppressed by all colors of light except red light. These two facts help to explain why people who work at night and sleep during the day, and people who live in metropolitan areas where nighttime darkness is diminished are more prone to cancer. So, when you are sleeping, no matter whether it is in the day or the night, be sure that your bedroom is completely dark. Ideally, you should not be able to see your hand in front of your face. Any light, except red light, needs to be eliminated. This includes light from LEDs, night lights, your clock radio, etc. One simple approach is just to cover the lights with a black cloth or tape. And be sure to buy some red night lights, so that you don't kill yourself going to the bathroom. That would completely negate the whole plan.

Unlike what is commonly taught, melatonin is not a soporific. That means that it doesn't make you sleepy. What makes you sleepy is darkness. When it is dark, your brain releases melatonin, and the melatonin sensitizes you to this effect of darkness. This is why older people, with melatonin levels close to

zero, have all kinds of sleep disorders. It's also explains why you can take it during the day and not get sleepy. I routinely prescribe my patients with stage four cancer 60 mg of melatonin four times a day – breakfast, lunch, dinner, and before bed. And only rarely does anyone tell me that it makes them sleepy during the day.

Melatonin is completely free of any significant side effects. Even after 50 years of study, scientists still cannot find an LD50 dose for melatonin. That means that it has no observable toxicity at any dose. Dr. Pierpaoli, one of the world's leading melatonin researchers, has successfully used daily dosages of melatonin in patients ranging from 0.1 to 200 mg. That's a 2,000-fold difference between the lowest dose and the highest. Studies on mice show that even at astronomical doses of 300 mg per day for two years there were no side effects. This is a dose equivalent to 45,000 mg per day in humans! Occasionally, a patient will report sleep disturbances or drowsiness in the morning, but more often than not, that is due to contaminated melatonin. Melatonin is a very delicate molecule. It must be carefully processed. Pressing it into a tablet and other methods of supplement manufacturing often destroys or alters the molecule. I recommend that you only use either pure melatonin powder or melatonin capsules that are free of additives.

One of the concerns that some people have about taking high doses of melatonin is that it can cause the body to stop its own production of the hormone. This concept is called negative feedback inhibition, and it is true of most hormones. But unlike other hormones, there is no negative feedback inhibition with melatonin. You can take as much as you want, and it will not interfere with your own production of melatonin. Additionally, melatonin supplements do not alter the levels of any other hormones.

In my conversations with Russell Reiter, PhD, the world's leading melatonin researcher, I learned that he has been taking 180 mg of melatonin every night for the past 18 years. At age 83, he is still running a laboratory and

working as a fulltime researcher. He has boundless energy and a brain that is as sharp as ever. When I asked him why he took so much melatonin he gave me two answers. First, 180 mg is the dose for a human that is equivalent to the dose that is so effective in animals. The other reason is that there is absolutely no down side to taking even these large doses.

Conclusion

So, should you be taking melatonin even if you sleep well? If you are older than 40, I say yes. The data that I have presented to you from 19 different papers on melatonin speaks for itself and is just the tip of the iceberg. But don't you need to check blood levels? Not if you're older than a teenager. The body peaks out in melatonin production during puberty. After then, it's all downhill. By the time you hit 20, you're already becoming deficient in the hormone. Studies on the urinary metabolite of melatonin, 6-sulfatoxymelatonin, a good indicator of how much melatonin your body is making, show that it decreases steadily with age. By the time you're 50, your levels of production are seriously low. So, if you want to have all of the benefits of melatonin, you're just going to have to take it as a supplement.

There are two sources of high-quality melatonin that I recommend. One is the pure bulk powder. You can get this at www.purebulk.com. They also sell a scale that will allow you to measure out the amount that you want. The other source and the one that I prescribe to my patients is called Melatonin Max. You can get it at www.perfectvitaminproducts.com. At 60 mg per capsule, it is the most powerful melatonin on the market. If you are over

fifty, I recommend that you do as Dr. Reiter and I do, take 180 mg every night before bed.

Reference

1. Srinivasan V, Mohamed M, Kato H. Melatonin in bacterial and viral infections with focus on sepsis: a review. *Recent Pat Endocr Metab Immune Drug Discov*. 2012 January;6(1):30-9.
2. Silvestri M, Rossi GA. Melatonin: It's possible role in the management of viral infections—a brief review. *Ital J Pediatr*. 2013 October 3;39:61.
3. Paredes SD, et al. Protective actions of melatonin and growth hormone on the aged cardiovascular system. *Horm Mol Biol Clin Invest*. 2014 May;18(2):79-88.
4. Scheer FA, et al. Daily nighttime melatonin reduces blood pressure in male patients with essential hypertension. *Hypertension*. 2004 February;43(2):192-7.
5. Vinther AG, Claesson MH. The influence of melatonin on the immune system and cancer? *Ugeskr Laeger*. 2015 May 18;177(21).
6. Bellipanni G, et al. Effects of melatonin in perimenopausal and menopausal women: a randomized and placebo controlled study. *Exp Gerontol*. 2001 Feb;36(2):297-310.
7. Obayashi K, et al. Physiological Levels of Melatonin Relate to Cognitive Function and Depressive Symptoms: The HEIO-KYO Cohort. *J Clin Endocrinol Metab*. 2015 June 8;e20151859.
8. Sarlak G, et al. Effects of melatonin on nervous system aging: neurogenesis and neurodegeneration. *J Pharmacol Sci*. 2013 September 20;123(1):9-24.
9. Wade AG, et al. Add-on prolonged-release melatonin for cognitive function and sleep in mild to moderate Alzheimer's disease: a 6-month, randomized, placebo-controlled, multicenter trial. *Clin Interv Aging*. 2014 June 18;9:947-61.
10. Naskar A, et al. Melatonin enhances L-DOPA therapeutic effects, helps to reduce its dose, and protects dopaminergic neurons in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinsonism in mice. *J Pineal Res*. 2015 Apr;58(3):262-74.
11. Parandavar N, et al. The Effect of Melatonin on Climacteric Symptoms in Menopausal Women: A Double-Blind, Randomized Controlled, Clinical Trial. *Iran J Public Health*. 2014 Oct;43(10):1405-16.
12. Vijayalaxmi, et al. Melatonin and radioprotection from genetic damage: in vivo/in vitro studies with human volunteers. *Mutat Res*. 1996 Dec 20;371(3-4):221-8.
13. Stefanova NA, et al. Potential of melatonin for prevention of age-related macular degeneration: experimental study. *Adv Gerontol*. 2013;26(1):122-9.
14. Blasiak J, et al. Melatonin in Retinal Physiology and Pathology: The Case of Age-Related Macular Degeneration. *Oxid Med Cell Longev*. 2016; 2016: 6819736.
15. Mills E, et al. Melatonin in the treatment of cancer: a systematic review of randomized controlled trials and meta-analysis. *J Pineal Res*. 2005 November;39(4):360-6.
16. Ma C, et al. Protective and sensitive effects of melatonin combined with adriamycin on ER+ (estrogen receptor) breast cancer. *Eur J Gynaecol Oncol*. 2015;36(2):197-202.
17. Sanchez-Barcelo EJ, et al. Melatonin uses in oncology: breast cancer prevention and reduction of the side effects of chemotherapy and radiation. *Expert Opin Investig Drugs*. 2012 Jun;21(6):819-31.
18. Lissoni P, et al. Decreased toxicity and increased efficacy of cancer chemotherapy using the pineal hormone melatonin in metastatic solid tumour patients with poor clinical status. *Eur J Cancer*. 1999 Nov;35(12):1688-92.
19. Sainz RM, et al. Melatonin reduces prostate cancer cell growth leading to neuroendocrine differentiation via a receptor and PKA independent mechanism. *Prostate*. 2005 Apr 1;63(1):29-43.

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