How Melatonin Combats Aging

A Pioneering Doctor's Ideas And Clinical Experience

By Saul Kent Founder

In the mid 1960s--in my early days as an immortalist--I met a young scientist named Paul Segall who had decided to devote his life to research to extend the human life span. Paul was the first scientist I'd ever encountered who had confidence that safe and effective methods to control the aging process would be developed.

At the time, Paul's focus was on experiments by Dr. Richard Gordon at the Monsanto Chemical Company, in which the life span of both chickens and rats had been extended radically by feeding them a diet deficient in the amino acid tryptophan. These experiments were a variation of the ground breaking food restriction experiments first conducted by Dr. Clive McCay at Cornell University.

Paul was fascinated by a small, mysterious organ at the center of the brain called the pineal gland, which he believed was involved in aging in some important way. This was shortly after it had been discovered that the pineal gland secretes a hormone called melatonin, which governs the circadian rhythms that help us adapt to changing environmental conditions.

A Biological Time Bomb

Paul believed that the human body is a biological time bomb with an intrinsic clock mechanism that causes us to grow old, suffer, and die with precision. He envisioned a genetically determined clock controlled within the brain through the action of the neurotransmitters, hormones, and enzymes of our neuroendocrine system.

In Paul's vision, the ticking of this clock is expressed through timing mechanisms that cause us to go through growth, puberty, and menopause at roughly the same time in the life span, and by the progressive deterioration of our cells and organs, leading inexorably to disability, decrepitude, degenerative disease, and death!

Dr. Segall's Research

Dr. Segall went on (in the 1970s) to explore the life span extension potential of tryptophan deprivation (T-) experiments in laboratory rats at the University of California at Berkeley. He found that T- rats were more youthful and lived longer than normally fed animals and that their extended youth could be shown by their improved ability to adapt to various types of stress, such as swimming in cold water.

The most dramatic illustration of youth prolongation in tryptophan deprived rats that came out of Segall's work was the finding that old (28 months of age) T- female rats were able to give birth to normal offspring at advanced ages, comparable to a 70 year old woman giving birth to a healthy baby.

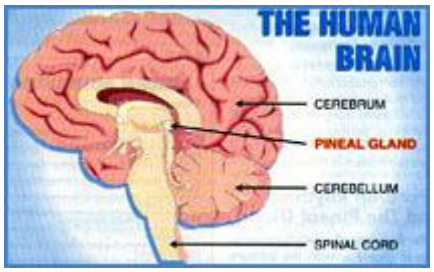
In conducting his T- experiments, Paul explored changes in brain neurotransmitter levels in his experimental animals, but never again focused on the pineal gland, which had fascinated him in the 60s.

In the 1980s, Paul turned his attention to Suspended Animation and began conducting low temperature experiments in hamsters and dogs through a company called Cryomedical

Sciences. Paul and his fellow scientists soon left Cryomedical to form a new company called BioTime, which extended this work to nonhuman primates (baboons). BioTime is now a public company seeking to apply its research to clinical hypothermia in humans.

Dr. Rozencwaig Focuses On Melatonin

Around the time Dr. Segall was losing interest in the pineal gland, a pioneering Canadian medical doctor by the name of Roman Rozencwaig was beginning to focus his attention on melatonin, the primary hormone secreted by the pineal gland.



Dr. Rozencwaig was born in Odessa in the USSR in 1946. He moved to Canada at the age of 14. He later obtained his medical degree from *McGill University* in Montreal, where he began experiments, which led him to the realization, in the mid 1980s, that melatonin plays a critical role in aging and the diseases associated with aging.

In 1987, Dr. Rozencwaig (along with B.R. Grad and J. Ochoa) published a seminal paper in Medical Hypotheses (Vol. 23, pgs. 337-352), in which he expressed his theory that the progressive depletion of melatonin with advancing age is a primary cause of aging and age-related diseases such as heart disease, stroke, cancer, and Alzheimer's disease.

In 1987, Dr. Rozencwaig began to treat patients with melatonin (as well as a drug with similar effects called Periactin . Dr. Rozencwaig recalls that:

"As a medical doctor, I first used melatonin in 1987 on a patient with lung cancer who had received all the standard therapies prior to the use of melatonin. Today, the patient is well, his metastasis has disappeared and he is leading a normal life. Since then many of my patients have benefited from melatonin and I have used it for various conditions with considerable success. Mainstream medicine is only now beginning to appreciate its value in treating various conditions."
For my practice, it has certainly opened a new vista in health care and rejuvenation."

Like Lightning Striking

The impetus for Dr. Rozencwaig's use of melatonin in clinical practice came as a byproduct of his pioneering ideas about the role of the pineal gland in aging and his realization that supplemental melatonin would likely be able to restore many of the life functions lost because of the atrophy of the pineal gland as we grow older.

He recalls that suddenly he experienced a vision of the role of melatonin in aging and that he knew from that point on that he would devote the rest of his life to helping people live longer by further exploring the role of melatonin in aging. As he puts it:

"It happened just like the popular view of how scientists make discoveries. It just came to me...without warning... like lightening striking! Immediately, started scribbling my ideas on the wall, so that I could preserve them in their original form."

Melatonin And Serotonin In Aging

Dr. Rozencwaig's hypothesis has been developed in several published papers. It was first expressed in his Medical Hypotheses paper entitled: The role Of Melatonin And Serotonin In Aging:

"Aging is a pathological process originating (from gradual failure) of the pineal gland that results in a diminished output of melatonin, along with a diminished melatonin to serotonin ratio, leading to a decline in adaptive processes....and subsequent death of the organism."

Circadian Rhythms And The Pineal Gland

Dr. Rozencwaig believes that the pineal gland is both the primary clock and pacemaker of aging, and that the time-dependent decline of our vital functions (aging) comes about as a result of the increasing disintegration of our neuroendocrine and immune systems. He believes that the harmony and consistency of these systems is maintained through bio rhythms, most of which follow 24-hour, circadian cyclicity (on our rotating planet) under the control of the pineal gland.

Dr. Rozencwaig contends that the pineal gland is:

"...a primary clock because it measures, and is synchronized with, the most constant environmental cue which is the light-dark cycle. The pineal's function as a pacemaker is carried out through the production of neurohormones, which subsequently control the entire nervous system and endocrine axis and hence homeostasis. This effect is achieved though (the secretion of) very small concentrations of substances produced in the pineal, primarily serotonin and melatonin."

Melatonin Is Produced From Serotonin

Melatonin is produced from serotonin with the help of several associated enzymes and co-factors, while serotonin is produced from the amino acid tryptophan, which is found in a wide variety of high-protein foods such as meat, fish, milk, and cheese. Melatonin is also found in small amounts in bananas, tomatoes, and other fruits and vegetables.

Melatonin also is produced in smaller amounts in the gastrointestinal (GI) tract and other parts of the body. The pineal gland contains the highest central nervous system concentration of serotonin in the body, and produces the largest amounts of melatonin as well as other neuroendocrine hormones.

Every day, as darkness sets in, melatonin production (from serotonin) in the pineal gland is rhythmically induced via cyclic AMP activation of beta receptors by the neurotransmitter norepinephrine through the action of the enzyme N-Acetyltransferase (NAT), which results in low levels of serotonin and high levels of melatonin, with a peak level occurring about 2 AM. During daylight hours, on the other hand, light entering the pineal gland through the eyes, blocks NAT's induction of melatonin, which results in high levels of serotonin and low levels of melatonin.

The Serotonin/Melatonin Ratio

The pineal gland has weak regenerative abilities because its primary cells (pinealocytes) are of neuronal derivation. The number of pinealocytes in the pineal gland is genetically predetermined, and these non-dividing cells are not replaced when they are lost due to biological or chemical injury.

"As we grow older, our pineal gland atrophies, eventually reaching a state of organ failure, as cells are constantly lost for a variety of reasons. The decline of the pineal is accelerated by the accumulation of calcium deposits, which cause the organ to harden and interferes with its activities.

According to Dr. Rozencwaig, the age related decline of the pineal gland means that there are fewer and fewer pinealocytes available to produce melatonin from serotonin, which leads to lower levels of melatonin and higher levels of serotonin, and that the resulting change in the serotonin/melatonin ratio is responsible for much of the deterioration experienced throughout the body with advancing age.

He points to evidence that increasing levels of circulating serotonin may be responsible for the increased incidence of certain types of cancer, and that high levels of serotonin are associated with platelet adhesiveness leading to atherosclerosis, the primary causes of heart attacks and strokes.

He also points to Dr. Segall's tryptophan-deprivation experiments, which, he believes, lowered only extra pineal serotonin levels, leading to a major decrease in the incidence of cancer and other degenerative diseases, as well as extended life span and reproductive capacity in laboratory rats.

The Regenerative Ability Of Melatonin

In 1987, when Rozencwaig, at al. published their hypothesis about the role of melatonin in aging, there was relatively little evidence to support it. Yet the extent to which they anticipated future research advances is remarkable.

It was pointed out, for example, that night is the time of replenishment, when our bodies recuperate by regenerating our tissues and restoring our glycogen reserves. Since melatonin is the natural agent that prepares us for sleep and circulates in peak amounts while we sleep, it almost certainly plays a major role in the regenerative process. The fact that melatonin is extremely effective at penetrating the blood-brain barrier indicates that it may be especially beneficial in the repair, regeneration, and rejuvenation of the brain during sleep. Among the anti-aging effects of melatonin mentioned by Dr. Rozencwaig in the 1987 paper is the fact that melatonin stimulates natural antioxidant levels, improves DNA repair mechanisms, and enhances our neuroendocrine and immune systems.

In a subsequent update in Pscyhoneuroendocrinology (Vol. 18, No. 4, pgs. 283-295, 1993) Grad and Rozencwaig discuss the evidence in support of their hypothesis. Among the effects of melatonin discussed in this paper is its ability to block pregnancy, boost immune function, improve the quality of sleep, regulate the endocrine system, protect against cancer, stimulate natural antioxidants, and protect against cardiovascular disease by inhibiting platelet aggregation and ischemia. (A review of the latest evidence for melatonin as an anti-aging therapy will follow this article).

The final paragraph in the paper is a cogent assessment of a theory of aging that time, and experimental evidence, is validating to a greater degree with every passing year.

"The Melatonin Deficiency Syndrome is perhaps the basic mechanism through which aging changes can be explained in terms of a single causative lesion, a lesion that causes the progressive patterns of change seen in the older population. In addition, pineal rhythmicity is the only biological clock synchronized with a time dimension, which also has the capacity to repair and rejuvenate the organism. Since the pineal gland's action to delay development is known, it is not surprising that it would also act to delay developmental senescent changes and extend the life span. In addition, it raises the possibility of the reversal of senescence....This may require replacement of melatonin along with other hormones in order to achieve a more youthful endocrine balance and homeostasis, and consequently a possible repair of the body as a whole."

The Melatonin Doctor

Dr. Rozencwaig has been treating patients with melatonin for about eight years.He's used melatonin for the treatment of cancer, inflammatory diseases, neurologic diseases, and viral diseases. He's had articular success with cancer patients, in conjunction with traditional treatments. Among the types of cancer he's treated are pancreatic, breast, brain, and lung cancer. When used as an adjuvant treatment for cancer, melatonin reduces the side effects of toxic therapies and boosts their effectiveness.

According to Dr. Rozencwaig, 36 mg of melatonin a day is sufficient if there is no metastasis, but if cancer patients have metastatic lesions, he doubles or triples their dose of melatonin.

The Case Of Dora Lewenstein