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INTERVIEW

Roman Rozenzwaig, M.D. is a pioneer in research on melatonin and aging. He was the first to postulate the theory that aging is a syndrome of melatonin deficiency resulting from the gradual failure of the pineal gland. Besides his continued anti-aging research, Dr. Rozenzwaig has been treating patients with melatonin and cyproheptadine for a wide variety of diseases and conditions, including lung and prostate cancer, Lou Gehrig's disease, Alzheimer's disease, AIDS, heart disease and stroke. Dr. Rozenzwaig practices in Montreal, Canada. He is on the staff at Reddy Memorial Hospital and Bishop Medical Centre in Montreal.

His new book, written with Hasnain Walji, Ph.D., and published by Hohm Press, is called *The Melatonin And Aging Sourcebook*, a comprehensive work that covers melatonin in research and clinical practice, with illustrations and an extensive bibliography.

This interview first appeared on the website of Mediconsult. It was conducted by Elsie Wagner, a Senior Medical Editor at Parkhurst Publications in Montreal. It is reprinted with her permission.

EW: What is the most important factor with regard to melatonin and aging: the absolute quantity of the hormone or the ratio of melatonin to serotonin?

RR: Both are important. Everything in life is relative, and a small increase in serotonin combined with a small decrease in melatonin can mean a quite dramatic change in the ratio between the two, and therefore in the signal that is transmitted.

EW: Your paper ("The role of melatonin and serotonin in aging: Update" [Psychoneuro-endocrinology, 18(4) :283-95, 1993] co-authored by B.R. Grad) states quite definitely that the pineal gland governs aging. In your opinion, just how important is melatonin in these processes?

RR: It is the key signal. My assistant, Adam Bly, and I have just finished an experiment using rotifers, which are single-cell organisms that live for five days. When we added melatonin to one group of rotifers from day one, their lifespan was double that of the group that received none.

We had various groups of rotifers under different regimens of melatonin, but the average lifespan increase was in the order of 70%-to-75% over those receiving no melatonin. In addition, the pineal gland produces other melatonin-like substances in minute amounts, which we believe are used in fine-tuning the mechanism.

I believe that over the next 50 years, as we learn more about the pineal gland, we are going to see human lifespans extend to the point where 150 years is not unusual. Many of my colleagues in this field feel the same way, though they may not have the courage to say so. Studies done by Dr. Smith found that any animal that is dead has a melatonin level of zero. That doesn't necessarily mean, of course, they if they had melatonin they would be alive. But it does suggest that when you run out of melatonin, you run out of life.

We can regard melatonin as a kind of master hormone, which governs other hormones and bodily processes by acting as a neurochemical transducer. The pineal gland has been called the third eye, and indeed, in some reptiles, it actually sticks out of the body as an eye. In humans and other animals, it has receded into the body, but it still "looks out" via neurologic pathways, and translates environmental conditions into a biological signal: melatonin.

EW: Some of the melatonin experiments reported in the literature, particularly rodent experiments, looked at animals that had their pineal glands removed, or at strains that were melatonin-deficient. Does the fact that restoration of normal levels of melatonin prolongs life necessarily mean that above-normal levels would prolong life longer than normal?

RR: First, you have to ask the question: what is a normal level of melatonin? Melatonin is a hormone that is present at very high levels during childhood, and begins to drop off immediately after puberty. From that point on, it's a straight line of decline all the



way to 120 years of age, at which age nobody still produces melatonin. The idea is not to supplement melatonin to abnormal levels, but to supplement it to what would be normal levels in, say, a 20-year-old. Then your other hormones and cycles will fit into that 20-year-old. Melatonin will trigger a response, but there is still some fine tuning necessary to get a full response.

EW: What, then, is aging? Is it an inevitable process, or is it a kind of programmed self- destruction?

RR: There is nothing inevitable about aging. Look at the trees that live thousands of years, and that have seeds that are still alive, in some cases, over two million years later. Theoretically, there's no reason for cells to stop regenerating, unless we run out of the substance that signals them to do so.

There is a debate on whether or not the body is programmed to self-destruct. Personally, I don't believe it and some take the view that there is no defined, finite life span. If you're a physician you see people who are dying from cancer, for example, and who weigh 80 pounds, and then they recover. Many people who almost died of hunger in concentration camps are still alive 50 years later and in good shape. We have an incredible capacity to regenerate, the question is: how can we harness that capacity?

EW: Can cells be made to regenerate indefinitely?

RR: I believe that they can. Even though Dr. Leonard Hayflick, a great authority on aging, suggested that a cell can divide only a maximum of 50 times, we should recall that he studied a particular kind of cell-not a very important one- and perhaps, more importantly, never changed the medium in which it lived, including food and waste products.

Theoretically, you cannot only stop aging with melatonin, but actually reverse it. This has in fact been done in practice to a certain extent. Recent research has shown how, when pineals are taken from young animals and transplanted into old animals, and vice versa, the old animals became young and started to produce offspring, and the young animals became sick and died. Of course, it can't make you regress into childhood! But theoretically, it could take a person back to a point where their body is like that of a young adult, which is the optimal point of human existence in terms of mature health.

EW: How are melatonin supplements taken?

RR: First of all, they should be taken only at night. Taking melatonin during the daytime can cause it to have effects opposite to those desired. It can, for example, actually increase rather than reduce the risk of cancer. I personally take melatonin regularly and begin with a dose of 3 mg at sunset, followed by another 3 mg just before going to bed.

Some people say that's a very high dose, but when you compare it with the 300 mg given in melatonin birth control pills, it doesn't seem like so much. Because melatonin has a very short half-life in the human body, most of it will be eliminated in the urine anyway, but first much of it is metabolized into a derivative called 6-hydroxymelatonin, which has melatonin-like effects. That means that the hormone has a kind of double hit or second passage through the body.

EW: Do melatonin supplements have any side effects?

RR: Here are a few. First of all, it acts as a contraceptive, certainly in women, and perhaps also in men. Theoretically, it should lower sperm counts, but studies have not yet been able to prove this effect in practice. It's an interesting phenomenon, because one of the questions about melatonin is: what will happen to the Earth's population if people start to live dramatically longer lives? And the answer is that there will not be a population explosion because melatonin has a built-in safety factor, if we can put it that way, because of its contraceptive effects.

There is currently a study taking place in about 2,000 women who are taking melatonin for birth control, in a massive dose of 300 mg per day combined with progesterone. This contraceptive effect has been studied now for at least two years. It's been proven that melatonin contraceptives actually protect against breast cancer.

Another side effect is that melatonin can produce quite vivid dreams, and that may mean the occasional nightmare. People who are manic (who have bipolar disorder) will tend to become more manic; it's not a good hormone for people who are in a psychotic state.

Finally, people with autoimmune diseases, in which the body attacks its own cells, should not take melatonin because the hormone tends to stimulate the immune system. These diseases include rheumatoid arthritis, multiple sclerosis, lupus and scleroderma, which are not particularly common compared to the diseases that cause the majority of deaths: cancer, atherosclerotic heart disease and strokes.

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