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Many researchers see promise in at least one dietary supplement, but others remain cautious

Can we 'die young as late as possible' thanks to a pill?

By Sean D. Hamill
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Pittsburgh neurosurgeon Joe Maroon has told the story of his health awakening many times, how he turned his life around when he was at his lowest.

He was 41, his wife had just divorced him and taken his kids, his father died, he temporarily quit neurosurgery, realized he couldn't even run one lap around a track without great effort, and he fell into depression.

Over the past 37 years, as he made changes to his physical and spiritual life and began to see the results — he has completed eight Ironman-length triathalons and continues to do surgery and see patients at age 78. Dr. Maroon became a proselytizer of how taking

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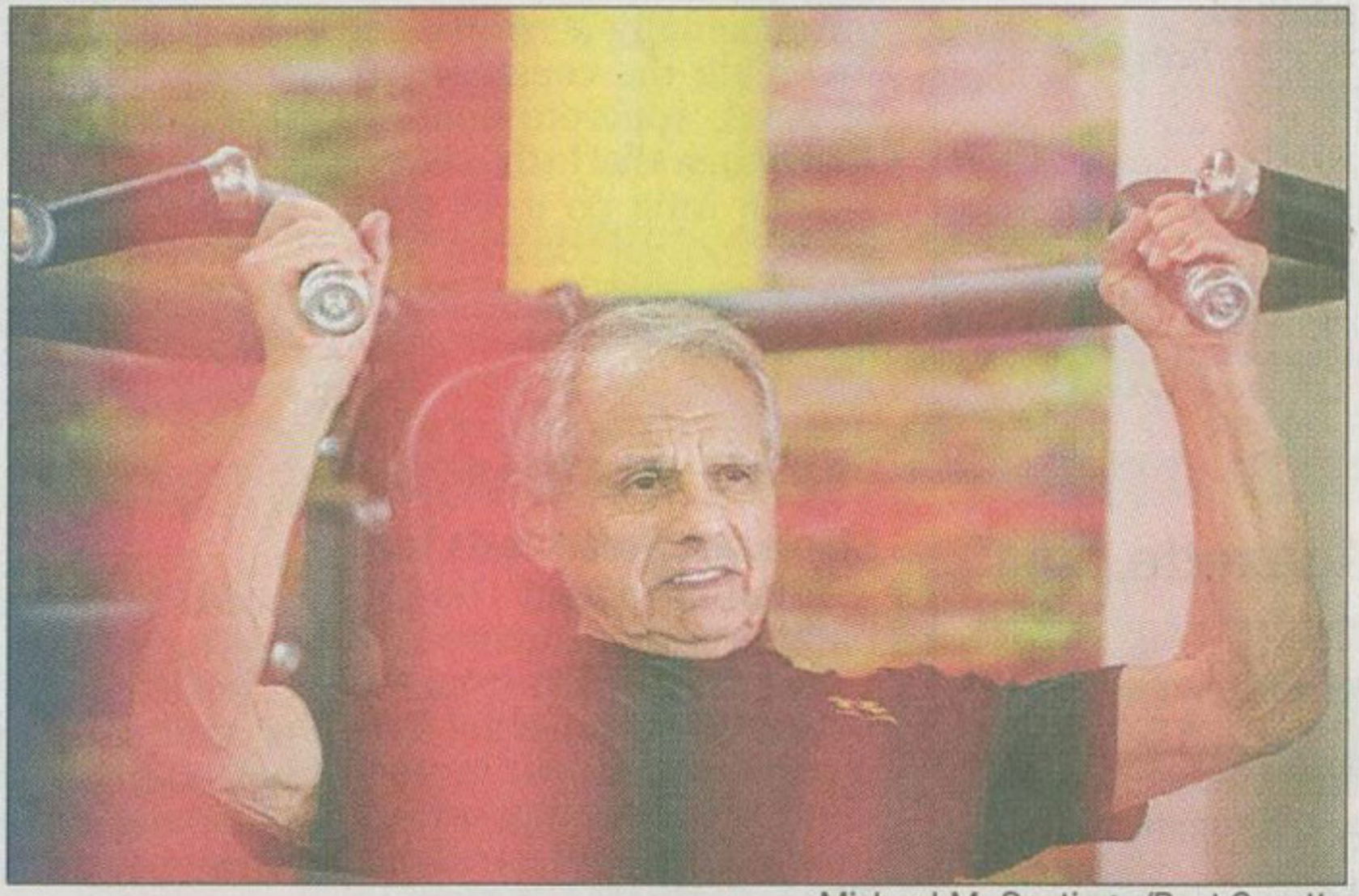

Michael M. Santiago/Post-Gazette

Neurosurgeon Joe Maroon works out at the Allegheny Country Club's exercise room on May 22 in Sewickley. For several years, Dr. Maroon has been taking a supplement called NR, which is said to boost NAD, a coenzyme in living cells that researchers believe may be a key to aging.

Research into dietary supplement focuses on the aging process

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care of the body can help take care of the mind. He has passed those lessons on to his patients directly and to others through lectures and five books.

Now he's taking his interest in exercise a step further.

Although he has been a prolific researcher during his long career — publishing nearly 300 scientific papers, nearly all of them related to neurology — for the first time he is embarking on a project to study the effects of a supplement on human muscle health.

It's a study asking a seemingly small, basic question, which is the way the hard, often plodding progress of research works.

But the supplement he wants to test — nicotinamide riboside, also known as NR, a vitamin form of B3 found in cow's milk and other foods — is part of a wave of research that ultimately asks a much larger question: Can we stall the aging process, or, at least, live healthier lives until we die?

It's the type of bigger question that jibes not only with Dr. Maroon's research interest, but his personal interest.

"Let me summarize my philosophy to you," he said in an interview recently in his office at UPMC Presbyterian hospital that is decorated with framed pictures of him competing in the Ironman (which involves swimming 2.4 miles, biking 112 miles and running 26.2 miles) in Hawaii. "My goal in life is to die young as late as possible."

NR is in the middle of this research wave — which includes research into other natural products that appear to have benefits to human health and longevity such as omega 3 fatty acids found in fish oil and resveratrol found in red wine, two areas Dr. Maroon also has looked into — because NR has been found to be a precursor to nicotinamide adenine dinucleotide.

NAD, as it is known, is a coenzyme in living cells that researchers believe may be a key to aging and age-related diseases. That's because coenzymes allow our body to work, including repairing DNA and making new cells. In animal experiments, NAD seems to have a particular benefit to mitochondria, known as the "powerhouse of the cell."

Since NAD levels have been shown to decline as we age, scientists want to know this: If you boosted NAD, would it boost the energy level of human cells?

Researchers already have found that NR can boost NAD levels in humans. Currently 18 human clinical trials involving NR are looking at everything from NR's impact on brain health to heart health and general metabolism.

Most of the studies are funded, at least in part, by two competing companies — ChromaDex and Elysium Health — that are engaged in a colossal fight over the patent that ChromaDex has for the manufacturing process of synthesized NR. The two companies sell a synthesized version of NR, either as a supplement — in ChromaDex's Tru Niagen product — or as a major component in a supplement — Elysium's Basis product.

NR has been approved as "generally recognized as safe" by the U.S. Food and Drug Administration, which means it can be sold only as a supplement, but not as a drug that can be marketed as treating, diagnosing, preventing or curing diseases. Both ChromaDex and Elysium hope additional studies will lead to drug approval, though.

Dr. Maroon and his co-researcher, Matt Darnell at the University of Pittsburgh's Neuromuscular Research Laboratory, are raising funding for this project, including from ChromaDex. Their aim is to see if taking NR improves human muscles.

Using two groups of adults who exercise, the study would give one group a daily dose of NR and the other a placebo. Muscle biopsies will be taken at the beginning and end of the study to examine whether the muscle cells' mitochondria benefit from the NR, whether there's an impact on the subjects' endurance, or if it only benefits adults who began with lower NAD levels.

Michael M. Santiago/Post-Gazette

Neurosurgeon Joe Maroon, 78, holds medals from various completed Ironman competitions at the Allegheny Country Club's workout room in Sewickley. Dr. Maroon is embarking on a project to study the effects of a supplement — nicotinamide riboside, also known as NR, a vitamin form of B3 found in cow's milk and other foods — on human muscle health.

Mr. Darnell, who has a doctorate in rehabilitation science, said he signed on to the study because he liked that it will try to get at so many questions, big and small.

"I'm not saying selling a supplement is a panacea," he said. "But it could be part of a lot of things to help you live healthier. This could be another tool in your toolbox."

Some have tagged this wave of research as a search for the fountain of youth in a pill.

That might sound like hyperbole. But Steven Austad, scientific director for the American Federal for Aging Research and a biology professor who studies aging at the University of Alabama at Birmingham, said taking a pill to live longer is not that far-fetched an idea.

"I think we will" have a pill like that, he said. "I think there's relatively little doubt. Maybe it's a statin that's effective against most of the results of aging, or something else. But there's a lot of fascinating stuff going on in the field now."

Some of that may come from research from the animal world that researchers like Mr. Austad, who has a doctorate in biological sciences, are doing.

For example, he is currently studying a species of clams that live up to 500 years. He's examining how they are able to prevent proteins in the cells from "folding," something that happens in humans as we age, leading to diseases like Alzheimer's.

Mr. Austad, who does not do research on NR or NAD, worries that trying to boost the energy in cells could have unknown consequences that have not been fully studied.

"It may cause your cells to start dividing, which would cause all sorts of chaos and could lead to disease," he said.

Despite that, he is still closely watching NR and NAD research, although he remains skeptical.

"It is interesting," he said. "But I just don't see the evidence at this point that [NR] is doing anything to improve life span."

Leonard Guarente, a biology professor at the Massachusetts Institute of Technology who is the co-founder and chief scientist of Elysium and has been doing research on NAD for 20 years, said improving humans' life span "is not our primary goal."

"We believe it could be used to forestall and maybe treat the major diseases of aging," he said.

His rival at ChromaDex sees the potential uses of NR similarly. Charles Brenner, is a biochemistry professor at the University of Iowa and chief scientific adviser at ChromaDex who first discovered the way to synthesize NR in a lab — it's that discovery that is at the heart of their legal battle — rather than extracting it from foods like milk.

"What we're trying to do in healthy aging is maintain muscle mass, cognitive function, heart function and overall health," he said. "And in animal models of animals with obesity, NR addresses fatty liver disease, it has improved function in diabetic neuropathy, protect against heart failure. There's a lot of potential benefits."

It is because of those animal studies that much of research in human clinical trials is focused on NR's impact on diseases or one aspect of health.

Rudolph Tanzi, a neurology professor at Harvard University and co-director of the McCance Center for Brain Health at Massachusetts General Hospital in Boston, said he joined the ChromaDex scientific advisory board last year because he likes the promise of NR for research into Alzheimer's.

He said he was excited by early research on lab mice with Alzheimer's that showed positive effects on the plaque that causes the disease.

"To be honest, though," said Mr. Tanzi, who has a doctorate in neurobiology, "it's pretty easy to fix an Alzheimer's mouse. Now we need to do it in humans."

He is raising funds to do a human clinical trial, testing to see if NR helps improve adults with Alzheimer's.

And that, he said, gets to his point about the larger field, which he hopes continues to focus on age-related diseases more than how long we live.

"I don't care about life span," he said. "I care about health span."

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