



News Home Page

Nation

World

Metro

Business

Washtech

Sports

Style

Education

Travel

Health

Alternative Care

Children & Youth

Chronic Diseases

Fitness

Health Care Issues

Men

Mental Health

Nutrition

Seniors

Women

Columns

Special Reports

Live Online

Photo Galleries

Health Index

Real Estate - NEW

Home & Garden

Opinion

Weather

Weekly Sections

News Digest

Classifieds

Print Edition

Archives

Site Index

Help

Time in a Bottle

Anti-Aging Boosters Claim Their Products Can Turn Back the Clock. Independent Scientists Aren't Buying It.

By Christopher Wanjek

Special to The Washington Post

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—More in Health—
• [Seniors](#)

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Would you like to grow younger, to turn back the clock 10 or 20 years and double your life span? Thanks to recent scientific advances, your chances are pretty good . . . if you're a parasitic worm or a fruit fly.

Humans, who for the most part are more complicated than these creatures, can reap no such benefits from the continuing flood of anti-aging potions and precepts, which are at best naively optimistic and at worst fraudulent and harmful. Yes, credible and independent scientists agree, medical research that now looks promising may someday lead to methods to slow the physical degeneration associated with aging and even extend the limits of the human life span beyond its current estimated 120 years. But, despite claims by those selling products and regimens, science hasn't done anything like that yet. For now, every book, powder or pill that promises a fountain of youth -- skin that doesn't age, organs that keep putting out, an immune system that never weakens, a mind forever sharp, a sex drive that never droops -- is just plain wrong: misguided, excessively hopeful or outright deceptive.

"There is no intervention that has been proven to slow, stop or reverse aging. Period," said Leonard Hayflick, professor of anatomy at the University of California, San Francisco, and a cult hero to many serious scientists in the field of aging.

Even Deepak Chopra, who has written several books about "reversing" the aging process, conceded in a phone interview that the most legitimate anti-aging therapies can only make you healthier, which reduces your risk of dying young -- but they don't make you young nor increase your life span.

"You can call it a question of semantics," Chopra said about his clients who feel and act younger than the typical person at their particular chronological age. This from a man who co-authored a book titled "Grow Younger, Live Longer: 10 Steps to Reverse Aging."

Chopra's conclusion -- that deadly disease risk can be minimized but life cannot be "extended" -- sounds obvious, but apparently few want to believe it. Other books, such as "Ageless Body, Timeless Mind" and "Renewal: The Anti-Aging Revolution" and "New Anti-Aging Secrets for Maximum Lifespan," have collectively sold millions of copies in recent years. Some

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researchers have promoted the use of, among other things, dog testes to extend age. Pharmacies, once content to sell hair dyes and wrinkle creams that cover up the signs of aging, are now hawking dietary supplements that purport to boost sex drive and return youthful vigor, some as basic as vitamin E and others as exotic as crushed deer antlers.

Web sites push products with names that would make Rambo proud, such as AgeForce Ultra Max 400 and Regensis Plus Recombinant GH. Hundreds of "anti-aging" clinics have opened across the United States in the past decade, charging clients upwards of \$10,000 a year for anti-aging hormone injections, an unproven and potentially dangerous therapy.

These naturally derived elixirs are not -- nor do they need to be -- approved by the Food and Drug Administration (FDA), a fact that prompted Sen. Larry Craig (R-Idaho), ranking member of the Senate Special Committee on Aging, to hold a hearing in September on phony anti-aging products. At the hearing, the head of one company failed to testify to defend his anti-aging supplement businesses or products. A September report from the General Accounting Office stated that some 40 percent of seniors take dietary supplements, many for conditions related to aging or for "aging" itself.

The GAO concluded that seniors face both physical and financial harm from to misleading marketing of such products. Sen. Craig's conclusion was that until stronger laws are enacted, people must educate themselves about anti-aging scams.

Bad Biomarkers

For this story, we have depended largely on the work of scientists and researchers who are independent of the various industries that sell anti-aging products and treatments to the public. One of the key independent voices in the field is S. Jay Olshansky, a researcher with the Center on Aging at the University of Chicago. He thinks much of the anti-aging medicine field is "pure quackery." Marketers are able to boast of age reversal, he said, because they rely on so-called biomarkers to measure the rate of aging.

These biomarkers -- handgrip strength, reflex time and blood flow, to name a few -- are only an indication of relative health, not age. Yet they are used to legitimize anti-aging therapies, he said. Techniques as simple as regular exercise and good nutrition can improve results in these very same biomarkers, providing a safer and far less expensive alternative to most anti-aging medicines and treatments. The problem is, there is no accepted way to measure aging, and everybody agrees that chronological age isn't a very useful standard.

There's a reason we cannot grow younger, Olshansky said, and it's called the second law of thermodynamics: Things fall apart. All matter -- and that includes your sack of bones -- moves gradually toward disintegration.

Aging as we know it is not a "process" that can be "reversed," he said. It is the result of an accumulation of damage at the molecular level over the years, an "inadvertent byproduct of a fixed program of growth and development," Olshansky said. Which is to say: Damage happens. Young bodies goof up as often and randomly as old bodies. A winding protein molecule might fold the wrong way, regardless of whether its host is young or old. A section of DNA

might not replicate correctly, regardless of whether you are 5 or 50. When this damage builds up, then you got troubles, Olshansky said.

A young body can repair itself more efficiently and keep damage to a minimum. This is true only because the repair mechanism itself -- like eyes, ears or any other part of the body -- hasn't had time to be compromised by molecular damage. Yet even if we could transplant a youthful repair system into an aging body -- which we can't -- that repair system would be just as overwhelmed tackling the backlog of molecular damage that naturally accumulates.

We can, through exercise, recuperate loss of vitality and physical capability due to inactivity, but not the kind due to aging, according to Walter Bortz of Stanford University Medical School, past president of the American Geriatric Society.

"Much of what we think about aging is not aging but disuse," Bortz said. He describes "disuse" by citing a leg in a cast. The leg shrivels, weakens and looks old, but it didn't really "age." With exercise, the old-looking, old-functioning leg can become vital and active again. But it can't get "younger."

Bortz said that the minimal damage accumulated at the molecular level resulting in a decline in overall physical ability is about 0.5 percent per year after about age 30. This assumes that you keep in tip-top shape. (Several studies have shown that this rate matches the decline in performance in professional athletes after their peak.)

But "if you don't take care of yourself, you start decaying a la Archie Bunker at 2 percent per year," Bortz said. This rate of decline would make you a mess by age 65. Disuse leads to sagging muscles and skin, a lack of stamina and strength, or a weakened immune system -- all the nasty things we associate with aging.

As banal as it sounds, Bortz said exercising and eating a healthy diet are the only proven methods to "look and feel younger" and reduce your risk of dying or suffering from the age-associated diseases: circulatory disease, cancer, stroke, arthritis and osteoporosis. This is also the best way to boost your sex drive, which magazines constantly tell us needs boosting. (How do they know, anyway?)

An Injection of Youth

Hormone therapy, one of the mainstays of the anti-aging industry, has no proven effect on increasing life span, say the academic experts contacted for this story, and in many cases it may harm you.

Hormone therapy is nothing new. Cocktails of testosterone, human growth hormone (HGH) and synthetic versions of the adrenal hormone DHEA have long been the domain of bodybuilders. They are now being repackaged to baby boomers as youth injections. The premise is that replacing these hormones -- which are plentiful in our younger years but almost disappear as we age -- will restore youth.

"Hormone therapy is a terribly oversimplified idea," said Huber Warner, associate director of the Biology of Aging Program at the National Institute

on Aging. "People are willing to inject themselves with hormones for short-term benefits without having a clue what the long-term effect might be."

Yes, there may be benefits, both tantalizing and immediate. With HGH therapy, for one, patients reportedly build muscle mass, lose fat, gain strength and stamina, improve mental acuity, increase their sex drive and develop more youthful-looking skin, according to Warner. These are those biomarkers again.

There are several caveats. Benefits are not guaranteed. Also, to sustain what you've gained, you must keep up with these therapies or lose it all. This can be an expensive proposition, with basic hormone therapy as low as \$500 a year but rising, with the addition of HGH, to \$3,000 to \$10,000 a year. Besides, there have been no human studies that show the injections extend life. Mammal studies are not encouraging. For instance, mice lacking growth hormone routinely live 30 to 50 percent longer than normal mice, and mice that overproduce growth hormone live 30 to 50 percent shorter, Warner said.

It gets worse. Growth hormone fuels cancer in mice, as reported by Karoly Szepeshazi of the Tulane School of Medicine in 2001 in the journal *Endocrinology*. Apparently, HGH triggers the release of another hormone, IGF-1, known to stimulate cancer growth later in life. This well-publicized "smoking gun" animal study confirms the cancer-causing HGH-IGF-1 pathway previously seen in numerous test-tube experiments.

Another blow to HGH, the most popular form of hormone therapy, may come in the spring with the official release of a long-awaited study from Johns Hopkins University, a double-blinded, placebo-controlled clinical trial that followed 152 men and women.

In this study, funded by the National Institutes of Health (NIH), subjects over age 65 were given for 26 weeks either HGH alone; a combination of HGH with either testosterone (for the men) or estrogen (for the women); or a placebo. Mitchell Harman, now director of the Kronos Longevity Research Institute in Arizona, said he found a "sliver of good news" in the study. Some participants increased muscle and lost fat on HGH, he said, while some taking the combo saw a small increase in strength.

"That's the bright side," Harman said. "The dark side of the forest is that there were lots of adverse effects." He cites joint pains, carpal tunnel syndrome and glucose intolerance. Five of the women became diabetic. Also, the HGH therapy did nothing for bone strength, which is what it is most often prescribed for. Although just a "preliminary study with mixed results," Harman said that at this point, he would definitely not recommend HGH for healthy adults.

Other studies reveal that testosterone therapy may lead to an increased risk for prostate cancer and heart disease, said the National Aging Institute's Huber Warner. DHEA therapy is a tossup for now, with mixed bits of evidence of possible benefit and harm. As for melatonin, a hormone associated with sleep cycles, Warner says that one study a few years ago showed a positive effect, yet "the whole thing was blown out of proportion" and no convincing data since then support its efficacy. He calls books such as "The Melatonin Miracle" and "The Superhormone Promise," which highlights DHEA, "simply irresponsible."

A co-author of these books sharply disagrees. William Regelson, 76, professor of medicine at Virginia Commonwealth University (and a taker of hormone therapy himself), said there is "solid evidence in the literature" that both "melatonin and DHEA boost the immune system by enhancing interferon production." Because hormones are not patentable, he said, industry has been reluctant to fund large studies of their benefits, and NIH has not stepped forward with money, either. His only regret about popularizing hormones is that they are available too easily over-the-counter, not regulated by the FDA.

Warner says hormone therapy has its place, but not as the all-around miracle worker on "age" and health that many of its supporters describe. Estrogen replacement therapy in women reduces the risk of osteoporosis and, perhaps, heart disease. Yet this too comes with trade-offs: an increased risk of breast cancer, a type of uterine cancer and blood clots.

Not all hormone therapies come in the form of shots. Hormone "activators" and natural plant hormones sold as pills, powdered mixes and sprays in health food stores are cheaper than injections (only \$50 to \$100 a month) and marketed heavily at consumers of anti-aging products. But several factors make questionable the value of hormones, or hormone precursors, in a pill.

For starters, Warner said, hormones need to be targeted (via injections) for maximum effect. Like many supplements, they may pass through the body unused rather than being absorbed by the proper cells and utilized. Also, in this era of loosely regulated herbal supplements, bottled hormones vary greatly in quality, and none needs to be proven effective to appear on store shelves or Web sites.

And, as with many other dietary supplements, there are no solid, independent, long-term studies in a human population proving the value (and the absence of serious side effects) of such pills.

Antioxidants for Life?

The idea that the physical characteristics, or phenotypes, of aging are the result of cumulative free-radical damage -- and that kinds of chemicals known as antioxidants can mop up these radicals to retard aging -- is very prominent in anti-aging products and literature. But this notion is also oversimplified and as likely to do harm as good, independent researchers say.

A free radical, a natural byproduct of metabolism, is an atom with an unpaired electron. Looking for a mate, it steals an electron from the first thing it encounters -- a cell wall, say, or a strand of DNA. The theft can cause these structures to malfunction, explained Britton Chance, professor emeritus at the University of Pennsylvania and an expert on free-radical production.

Antioxidants are a class of chemicals that render free radicals benign. The popular antioxidants are vitamin C and E, selenium, beta carotene and, especially for the anti-aging crowd, coenzyme Q-10. What remains far from certain is whether these antioxidants taken in the form of dietary supplements can pass through the human digestive system and go exactly where duty calls, to the site of free-radical attack, Chance said. Studies have shown positive, neutral and negative effects of antioxidant supplementation. Studies on antioxidants derived from diet lean more positively, but even there longitudinal data suggest that an antioxidant-rich diet reduces the risk of some diseases,

rather than extends one's life.

Levels of coenzyme Q-10, which is produced naturally within the body and may collect free radicals almost as soon as they are created, decline with age. Yet as several studies have shown, only about 2 percent of a coenzyme Q-10 supplement reaches the bloodstream, and likely far less (if any) enters cells. Thus, scientists are far from concluding that boosting bloodstream levels of this coenzyme via supplements is a good thing at all, let alone a means to extend human life span.

Stopping free-radical damage would definitely be nice, Chance said. This would, by some researchers' definition, slow the "aging" process by at least arresting certain types of cellular and DNA damage. This is where caloric restriction -- perhaps the worst bad news to anti-aging enthusiasts -- comes in.

Starving for Longevity

Semi-starved mice and rats that get only 70 percent of their usual daily calories live, on average, 50 percent longer than their rodent friends on a normal diet. Why? The theory is that, at the molecular level, less food translates into fewer energy conversions, slower metabolism and thus fewer free-radical byproducts to wreak havoc.

This is, once again, an oversimplification, and researchers know it. The trouble is that the rodents and, it now seems, semi-starved monkeys, don't know it. They actually appear to be aging more slowly and leading normal lives, some scientists say. Caloric restriction, however unappetizing an idea, is the one intervention that very well may slow down the human aging process and increase human life span beyond 120 years, said Walter Bortz of Stanford.

Yet caloric restriction remains unproven as an age extender in humans. Rodent studies are not necessarily applicable to humans because scientists can manipulate their life spans in a variety of ways. The monkey study has intrigued many scientists, but monkeys live about 40 years, and scientists still have another 20 years to go to see whether these animals really live any longer. There is no way to truly know whether the monkeys are aging more slowly, said Hayflick, the anatomy professor in San Francisco. This, once again, is a reflection of the lack of legitimate biomarkers to measure the rate of aging.

Besides -- and this is the reality check demanded of anti-aging recommendations -- if consuming 70 percent of current recommendations throughout your life extends it for, say, a couple of decades, who's going to stick to that diet for an increased likelihood (but no guarantee) of that payoff?

The Promise of Genes

Thomas Perls, a longevity expert at Beth Israel Deaconess Medical Center in Boston, is trying to prove the existence of longevity-enabling genes. These genes might prevent cancer and heart disease, allowing you to live to an older age, or they might somehow slow the production of free radicals or do a better job at repairing the damage.

"We don't yet know what longevity-enabling genes do," Perls said, but he has found a possible set of age-enhancing genes on chromosome 4 in his massive study of centenarians. There can be no gene that controls life span itself, Hayflick said, because such a gene would have no way to be selected and passed on from generation to generation. Genes for quickness or good eyesight or sexual capacity are refined and passed on because they are useful for the animal to survive long enough to reproduce. A gene to live to 100 cannot evolve through the process of "survival of the fittest" unless we humans reproduce at age 100 (perhaps one of the scariest ideas in all of anti-agedom).

Instead, centenarians get to that grand old age of 100 by avoiding disease, not by a gene that keeps them ticking for unusual lengths of time. Maybe they had genes that helped, Perls said; maybe they got lucky. Regardless, gene therapy -- whenever that day might come -- would only allow more people to live out their natural life spans, not live significantly longer lives. Use genetic tweaks to cure the feared killers of the aged -- cancer, heart disease, stroke and Alzheimer's (and doctors are not even close to accomplishing this) -- and you have boosted life expectancy to about age 95, Hayflick said. You have still done nothing to change life span.

The claim that humans will, on average, live past 120 years -- a claim made by some of the proponents of caloric restriction and gene manipulation -- is not completely ungrounded. But it is premature. Scientists can make nematode worms live twice as long as usual by manipulating various genes. But you can make these millimeter-long parasites live longer just by looking at them the wrong way. These organisms, unlike humans, have the ability to enter into hibernation.

The same is more or less true with fruit flies. The more complex the animal, the less drastic the improvements in life span. Genetically engineered mice do not live much longer than other mice do.

In humans the issue is complicated, the University of Chicago's Olshansky said, because the same genes that allow us to live at all (those that help us hunt, see, reproduce) often lead to cancer and other diseases later on. This is called antagonistic pleiotropy, and it may explain the existence of aging itself, for evolution cares only about getting you to reproduce and rear your young. Whatever works, works; the ill consequence 20 years later of a bad gene that did its job when it had to is tough luck.

Far in the future, scientists just may find a means to slow metabolism and reduce free-radical damage, perhaps through a friendly version of the caloric restriction method. Babies born today may, if the science progresses rapidly, be the first to benefit from life-extending therapies. Yet the science of aging is brand-new, and we may be as far from life span extension as physicists were from placing a man on the moon upon the discovery of the electron in the late 1800s.

"With every generation you have scientists making some claim -- that we're very close to unlocking the secrets of aging, the fountain of youth," Olshansky said. "We're not."

Christopher Wanjek last wrote for the Health section about the benefits and risks of antioxidants.