Barbell Training is Big Medicine

by

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Rx: Fountain of Youth

For some time now, in the course of my duties as an emergency physician, I've had strange thoughts at the bedside of some of my patients. I'll approach a patient who has come to be treated for chronic pain, fatigue, elevated blood pressure, shortness of breath, or a blood sugar that's out of control. I find myself confronted by a very overweight, deconditioned 52 year-old, going on 70, with battered joints, atrophic muscles, no physiologic reserve, an inability to get off the gurney without groaning and wheezing, and a grim future. When I work them up, I find no medical emergency, just what I have come to call "diatensionolesity"—type II diabetes, hypertension, a screwed-up blood-lipid profile, and obesity.

And I think to myself: *If I could get you under the bar, I could change your life.*

Then I give them a lecture about their weight and their smoking, write a prescription for painkillers, blood pressure medicine, diuretics or an oral hypoglycemic, and send them back to their grim future. These immediate interventions are necessary, but what I really want to do, as a physician and a person, is to *alter* that future, to help them recover some of their youthful vigor, to reverse the atrophy and degeneration of their sick bodies. I want to make them stronger, or at least show them that it's possible to *be* stronger, and how to do it. I want to write a prescription for squats.

I think I have found a fountain of youth, and it flows out of a barbell.

I have both a personal and professional interest in aging. My personal interest is easy to understand: I'm getting older. I just turned 51. My joints are creakier, my hair is graying rapidly, and it seems like every week I need a stronger prescription for my reading glasses. My glands don't squirt like they used to. My metabolism, left to its own devices, would rather turn calories into fat and ear hair than hard muscle and bone. I work hard to keep my mind active and learning, because while I can keep adding synapses to my brain, the number of neurons in there will only continue to fall. *I'm over the hill.* Now the only question is how steep the slope is on my side of the mountain.

My professional interest in aging may also seem obvious: I take care of sick people for a living, and older people tend to get sick more easily, and succumb to illness more readily. But my interest goes beyond the clinical.

Sick Games with Cell Suicide and Growth Factors

Since 1995, I have been involved in cerebral ischemia research. This means that I investigate what happens to the brain when blood flow is interrupted, as happens in stroke or during cardiac arrest[1]. My focus is on molecular mechanisms that lead to brain cell death or survival. I'm not a particularly gifted or lucky or influential scientist. I'm just an obscure, poorly-funded ER doc doing part-time research in a basement lab, grinding away at my tiny corner of a huge problem: *what happens when the most complex object in the known universe gets sick, and how do we fix it?* In the course of this quixotic endeavor, I have learned a lot about how cells decide to die.

That's right. Most of the time, cells *decide* to die. It's not a passive process, but rather the culmination of an elaborate biomolecular self-destruct program called *apoptosis* or *programmed cell death*[2, 3]. Apoptosis is critical to advanced, multicellular life forms. Without it, embryonic development would be a disaster. Viral infections would spread like wildfire if cells weren't programmed to sacrifice themselves for the greater good when compromised. And apoptosis is one of the body's primary defenses against malignant transformation and cancer.

Apoptosis is horribly complex in the particulars, but the big picture isn't hard to sketch out. There are two basic pathways: *extrinsic* and *intrinsic*. In extrinsic apoptosis, another cell or tissue sends a death signal, a chemical message which is picked up by the target cell and tells it to die. In the intrinsic process, a stressor causes the cell's power plants, the mitochondria, to spill a protein called cytochrome *c* into the cytoplasm. Think of a leaky reactor—bad news. When cytochrome *c* oozes out of the mitochondria, it triggers a complex series of events that lead to apoptosis. In both intrinsic and extrinsic patterns, the terminal phase of apoptosis is carried out by proteases and nucleases—protein enzymes that cut up other proteins or DNA. These enzymes take the cell apart in an orderly fashion and clean up the mess.

At some point during apoptosis, the cell will become unrecoverable. It will be, in a word, *dead*. When the cellular organelles start to shrink up and disappear, there is little hope for the cell. And once a cell has started to cut up its DNA, it has blown its own brains out. Game over. However, because apoptosis is not a passive falling-apart, but a molecular *program*, one that has to be signaled, triggered, activated and executed, it can be modulated. Up to a point, apoptosis can be inhibited or reversed, and the most effective way to do so is through *growth factor signaling*[4].

Growth factors are peptide hormones like human growth hormone (HGH), insulin, insulin-like growth factors (IGFs), endothelial-derived growth factor (EDGF) and nerve growth factor (NGF), among many others. Like anabolic steroids, they induce a trophic effect. However, unlike steroids, peptide growth factors act through membrane receptors on the cell surface, activating a cascade of internal signals that promote growth.

But growth factors don't just promote growth--they promote *cellular survival.*

For example, you can subject cultured cells to any number of noxious stimuli that will not kill cells outright, but will cause them to snuff themselves. Such stimuli include hypoxia, radiation, chemicals like ceramide or arachidonate, certain types of viral infection, or overwhelming concentrations of calcium or free radicals, to name a few. The cells will promptly activate their self-destruct programs, shrivel up and die. However, you can slow down or arrest the apoptosis program by administering a

growth factor, such as insulin or IGF-1, to the culture. As a result of observations like these, growth factors are under intense scrutiny for their potential to treat a number of stubborn and devastating degenerative diseases, including stroke[5].

But that's not all. If you take cultured cells, which are growing in a nutrient serum, and you remove that serum, they will die, *without any other insult*. Why? Because the serum contains growth factors. Removal of growth factor signaling is sufficient to trigger apoptosis in many types of metazoan cells[4,6,7].

One (somewhat contentious) way of looking at this is that *the default mode of these cells is not to live, but to die*. If you remove growth factor stimulation, they will kill themselves. The death machinery is there, just waiting to be activated. The teleological, evolutionary, and philosophical implications of this observation are staggering…but beyond the scope of the present article. Today we're talking about aging, and barbells.

Apoptosis and aging: The Molecular Perspective.

Classic apoptosis and other forms of regulated cellular self-destruction seem to play a role in the biology of aging[8,9,10,11,12]. At the time of this writing, there is abundant evidence that programmed cell death is one of the mechanisms responsible for the neural degeneration, muscle atrophy, sarcopenia and osteopenia that descend on us like vultures in the second half of our lives. And there's increasing interest in the use of growth factors and other anti-apoptotic strategies to retard the loss of these critical tissues[13].

Let's take muscle atrophy (loss of muscle mass) and sarcopenia (loss of muscle cells) as examples. Muscle loss is endemic in older individuals, and it predicts frailty, illness, loss of independence, injury, and all-cause mortality[14]. The impact on health care costs is significant, and the impact on quality of life and human suffering is incalculable.

Myocyte apoptosis— muscle cell suicide—appears to be a key contributor to the muscle atrophy and sarcopenia seen in geriatric and sedentary populations[14,15,16,17]. High levels of pro-apoptotic proteins, including proteolytic enzymes, have been found in the atrophic skeletal muscles of aging rats, and the myocytes in these muscles demonstrate apoptotic changes, including DNA fragmentation. The data in humans, while limited, also implicates myocyte apoptosis as central to muscle loss. For example, older human subjects demonstrate large numbers of apoptotic muscle cell nuclei compared to controls[18].

The age-related loss of muscle tissue tracks a corresponding decline in trophic factors, including anabolic steroids and peptide growth hormones. For example, levels of IGF-1 fall with advancing age, and lower IGF-1 levels are thought to be causally related to the loss of strength and muscle mass that progresses as we grow older. Conversely, growth factors such as IGF-1 induce induce skeletal muscle hypertrophy[19]. Transgenic animals that have been engineered to "overexpress" IGF-1 show reduced age-related loss of both muscle fibers and motoneurons. Older individuals who are genetically predisposed to make more IGF-1 appear to make better gains on a strength-training program[20]. And a 2002 study observed an increase in muscle strength (and bone mass) when IGF-1 was administered to women recovering from hip fractures[21].

Observations like these led to a burst of studies investigating the administration of growth factors to older individuals[13,22,23]. The results trend toward improvement in lean body mass, decreased body

fat, some improvement in serum lipids, and increased strength. Unfortunately, they also indicated an increase in adverse events, including insulin resistance, diabetes, gynecomastia, joint pain, and swelling[23].

The take-home message here is that, while it may be tempting to take trophic factors as "supps" to retard the aging process, and while it *may* be beneficial to do so in older populations with more blunted hormonal responses, the ideal approach is to *make our own*, in our own bodies, for as long as we can, so that the responses are physiologic, regulated, and healthy.

When we train with a barbell and eat correctly, we are sending a signal to our body that an anabolic environment is called for. An anabolic environment means growth factors. Growth factors suppress apoptosis. And apoptosis is a fundamental part of aging.

That's my own *molecular* perspective. More correctly, that's a gross oversimplification of the molecular perspective. We haven't talked about the role of oxidative stress, calcium leak, telomere shortening, and other processes that appear to play a role in muscle loss and aging[24]. And of course, much of what we think we know about apoptosis and aging is, like any scientific model, provisional. It's important to point out that a minority of investigators don't believe IGF-1 mediates exercise-induced hypertrophy[25]. And disuse atrophy (non-age-related atrophy resulting from immobilization, unloading, spaceflight, etc) of skeletal muscle certainly appears to involve pathways other than classical apoptosis—although, like apoptosis, these alternative pathways still represent regulated "self-destruct" programs[26].

Much work remains to be done on aging, apoptosis, and muscle atrophy. But I've given you this molecular perspective because I really want to make a larger point. I think the *macro* perspective is even more illuminating. I maintain that apoptosis doesn't just occur on the cellular level. I think a similar process of self-destruction takes place at the level of the human being, and like cellular apoptosis it is accelerated by aging and aggravated by the withdrawal of trophic stimulation.

Call it *human apoptosis*.

Human Apoptosis

Aging is characterized by a loss of strength, flexibility, and adaptive physiologic reserve; by senescence of growth and repair systems, blunting of hormonal responses, and atrophy of muscle, nerve, tendon, ligament and bone. This physical atrophy is accompanied by an even more deadly psychological decline. Too often, the aging individual sees that he is getting weaker, and so lowers his expectations and his efforts—and thereby grows weaker still. This is analogous to the cell cutting up its own DNA. Once the psyche has surrendered to decline and death, it's all over but the suffering.

Like cellular self-destruction, I think human apoptosis also comes in both intrinsic and extrinsic flavors. Fortunately, we have seen a decrease in extrinsic "death signaling" to older people, with the growing acknowledgment that it is possible to remain fit and active well into our extended life spans. Still, aging individuals are told by cultural stereotypes, TV, family, doctors and other "experts" that they need to slow down, eat less meat, and for God's sake act their age. The intrinsic signals are even worse: "I'm fat. I'm weak. I'm worthless. My joints ache. And I'm too old to do anything about it. Where are the Cheetos?"

This is an increasingly prevalent phenotype of aging in America and other industrialized nations[27,28,29]: a living hell of progressive weakness, obesity, inactivity, shrinking horizons, sexual impotence, decreased expectations, mounting despair, a growing list of expensive drugs, learned helplessness, sickness, and pain. It's being "All Done At Sixty"…or Fifty. It's a life of waiting to die from a skin infection or a broken hip or a blot clot, of needing a stupid little fucking go-cart to get from here to there, of not being able to reach your own ass to wipe it, of narcotizing yourself with alcohol, cigarettes, *American Idol* and Doritos so you don't have to face your own grim existence as a slowly rotting Jabba The Hut. I see it every day. We call it "old-itis." A joke, I guess, but an obscene one. This gruesome avatar of aging offends the eye, the mind, and the spirit, and it cries out for both compassion and correction.

Strength training is a macroscopic growth factor, countersignalling *all* of this evil shit. This is not my wishful extrapolation of cellular phenomena to the human sphere. It's a medical observation, supported by study after study. Research with elderly subjects indicates that resistance training improves overall function and strength[30,31], enhances bone density and balance adaptations [32], and improves the metabolic profiles and glycemic control of patients with type 2 diabetes[33] . A landmark 2008 study of nearly 9000 men followed for an average of nearly nearly 20 years showed that muscular strength is *inversely associated with death from all causes,* even when adjusting for fitness and cardiovascular health[34].

That's *strength training*. What about barbell training? Like every other area of exercise science, research into strength training in the elderly under-represents barbell training. But I would posit that all of the well-known advantages of barbell training will be magnified in elderly populations. The basic barbell exercises train the largest amount of tissue, and will thereby evoke the largest systemic and local responses, including elaboration of trophic factors. Squats, deadlifts, and presses strengthen functional movements—getting up, walking, standing, bending over, reaching—that we all rely on every day and that can be challenging for deconditioned elderly people. And because, unlike machines, barbell exercises do not isolate joints and their corresponding tendons and ligaments in unnatural loaded movement patterns, we can expect them to be far less likely than machines to damage older, more beat-up joints.

Finally, barbell training, like any other medicine we would give an elderly person, is *titratable*. In fact, it is far more exquisitely titratable than most medicines. It can be dosed exactly, according to the needs of the "patient." But there is one crucial difference here that I must bring to your attention. Unlike other medicines, where an increase in dose corresponds to the patient getting *sicker*, the 70 year-old patient whose squat "prescription" goes from 195 to 200 lbs is getting *healthier*, and stronger.

That's the kind of prescription I'd like to write.

To the Last Rep

In a system (the aging person) whose default mode is to die, whose human apoptotic signaling is in place and activated, barbell training signals for survival and for growth. It forces muscles to grow stronger and more flexible, tendons and ligaments to become thicker, bones to start sopping up calcium and lay down new matrix, kinesthetic perception to get with the program, and endocrine systems to get off their ass. It negates the *extrinsic* form of human apoptotic signaling: every additional geezer who trains with a barbell is a living refutation of the stereotype of the frail senior, an example of what aging can and should be. More importantly, training blocks the *intrinsic* form of human apoptotic signaling, by sending a message to the gray goo in our head that yes, we *can* get stronger.

I'm not talking about a panacea here. Barbell training won't bring back your cartilage, improve your eyesight or shrink your prostate. Like the neuron or the lymphocyte talked off the ledge by a peptide growth factor, the individual who trains with a barbell cannot stave off death and disease forever. And training won't work for everybody—many individuals will be too debilitated or too moribund to train. Many more simply won't be willing—staying strong comes with a price, and that price is hard work. Much more research is needed to evaluate how barbell training is best adapted to senior populations, whether it can be safely potentiated by trophic factor supplementation in those with the most blunted hormonal responses, and the effects, if any, on psychosocial parameters, hospitalization rates, cognitive decline, sexual function, and chronic pain. The literature is woefully lacking in meaningful longitudinal studies conducted with proper methods.

And before you ask: at present there is absolutely no solid evidence that strength training—or any other exercise or dietary program—will substantially prolong our life spans. But the preponderance of the scientific evidence, flawed as it is, strongly indicates that we can change the *trajectory* of decline. We can recover *functional* years that would otherwise have been lost. There is much talk in the aging studies community about "compression of morbidity," a shortening of the dysfunctional phase of the death process. Instead of slowly getting weaker and sicker and circling the drain in a protracted, painful descent that can take hellish years or even decades, we can squeeze our dying into a tiny sliver of our life cycle. Instead of slowly dwindling into an atrophic puddle of sick fat, our death can be like a failed last rep at the end of a final set of heavy squats. We *can* remain strong and vital well into our last years, before succumbing rapidly to whatever kills us. Strong to the end.

That, my friends, is Big Medicine.

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