Why is EXERCISE GOOD for you?

Run your car hard and it breaks down. Run your body hard and it picks up. Our intrepid reporter investigates to find out why pain leads to gain.

BY JOHN BOHANNON

After tearing around the corner of Rossauerlände and outrunning the street tram like a madman, I was flying up Vienna's canal promenade on a wave of adrenaline, feeling magnificent, cocky. Then it happened. Did I push too hard? I doubt it. I've run the same sprint a hundred times. But by the time I hit the bridge over the Danube, I knew it was coming.

The pain has no specific address. It's more like an out-of-tune melody in a symphony, growing louder until everything sounds wrong. I got home and shuffled straight to the WC. And even though the times I've seen it number a dozen—and half as many doctors have concluded it's probably nothing to worry about—it still shocks me. There it goes, a bright red arc of blood-tinged urine making a horror show in the toilet.

Exercise is supposed to be good for you. In fact, according to decades of scientific research, failure to exercise can kill you. Those who indulge in a couch- and car-based way of life are much more likely to get bagged by the big killers: cardiovascular disease, diabetes, cancer. And yet, from a mechanical point of view, exercise is self-abuse. Microscopic muscle fibers rip, toxins flood your bloodstream, organs slosh and collide, skeletal joints bump and grind.

When things go wrong with my body—and they do; the technical term for last week's fright is runner's hematuria—I have to convince myself all over again. This time I decided to bolster my faith in exercise by getting to the scientific heart of the question: How can something that seems so bad do so much good?

Ask any engineer how to maximize a machine's life span and he or she will give the same advice: Use it gently and it will break down more slowly. The second law of thermodynamics—which says, in essence, that every system tends to run down—is bad news for machines. The more numerous and complex their parts, the more vulnerable they are to wear and tear.

Paradoxically, the opposite advice applies to the human machine: Use it too gently and it will break down more quickly. We don't disobey the laws of thermodynamics, of course. Instead we work around them by eating, excreting, and shedding heat. The net result is that we constantly rebuild ourselves while exporting our damage to the environment around us. Keeping that process going requires that we remain active.

The optimal level of human activity was shaped by our evolution, a quirky solution to the specific challenges faced by our Paleolithic ancestors. (Many scientists argue that the most common serious illnesses of the industrialized world, the "diseases of affluence," are due to a mismatch between the circumstances of modern and Paleolithic life.) But how many miles per day do my Paleolithic genes need me to run? To find out, I call Loren Cordain, a physiologist at Colorado State University at Fort Collins, who studies exercise and health from an evolutionary point of view. "There's no simple formula," he says, "but if health is the goal, the optimum amount of exercise is much more than you'd probably expect."

Cordain puts that ominous "much" into perspective by relating a story about one of his research collaborators, Kim Hill, an anthropologist at Arizona State University at Tempe. While studying an Amazonian tribe of hunter-gatherers called the Ache, Hill encountered Paleolithic exercise firsthand. It wasn't unusual for an Ache peccary-hunting party to go 8 to 10 hours, including long pursuits that required several hours of intense activity without a rest. Hill recalls in particular one hunting trip he joined in the 1980s: He was in great shape, but he barely made it to the end. His younger graduate students didn't manage at all.

"Of course the Ache didn't do that every day," Cordain reassures me. "A big hunt like that would be followed by some days of relaxation, and a more typical day adds up to between 5 and 10 miles of walking and running." Keep in mind that those are forest miles, not suburban sidewalk miles. And hunter-gatherer days are full of other physical exertions, such as butchering carcasses, scraping hides, climbing trees, and dancing. Cordain's take-home message: "The ancestral lifestyle is equivalent to cross-training for endurance sports like marathons and triathlons."

Studies that compare athletes, moderately active people, and full-on couch potatoes back that claim, Cordain reports. "Virtually any measurement we can make improves with exercise and gets worse the more sedentary we become." The bodies of athletes read like

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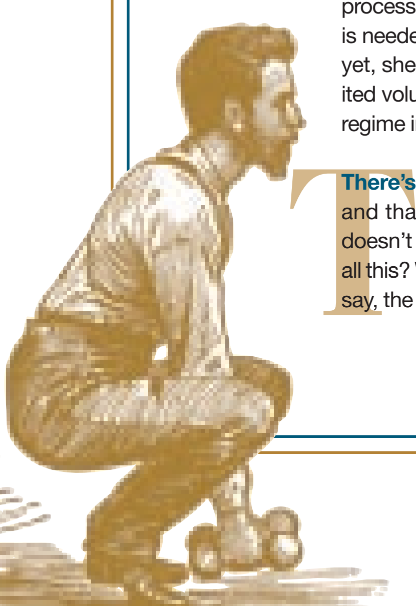
a physiology wish list. A regimen of regular exercise improves arterial function, blood lipid profiles, intracellular ionic concentrations, insulin sensitivity, and heart function—all of which seem to account for the disease-reducing aspects of exercise. Physical activity is even associated with lower risk of Alzheimer's.

So far, so good, but I still have a nagging doubt. How many of the benefits of exercise are psychological, not physiological? I know from experience that missing my daily sports can send me into a tailspin of bad sleep, bad eating habits, and grumpiness. That makes me wonder how much of the long-term health impact is due to avoiding the effects of depression. I put the question to Henriette van Praag, a neuroscientist at the National Institutes of Health who studies the effects of exercise on the brain. "Exercise does help prevent depression," she says, "even as well as anti-depression medications." But exercise is good for you whether you like it or not. "How about comparing military recruits, who are forced to exercise, with recreational runners?" she suggests. Other research has compared the health of mice forced to run on treadmills—which is stressful—with mice that go the same distance voluntarily on running wheels. "The outcome is quite similar," she notes. Besides improving indicators of cardiovascular health, exercise "reduces anxiety-related behaviors." As a bonus, "performance in learning and cognition improves."

You read that correctly. Exercise makes mice smarter—so much for the dumb jock stereotype. Fit mice get an "increase in new neurons in the hippocampus, a brain area important for learning and memory." And their neurochemistry lights up like a Christmas tree, with boosts in glutamate receptors (for learning), serotonin (for mood stability), and neurotrophins (for building new connections between brain cells). The growth of blood vessels (to feed those hungry cells) increases too.

As for humans, so far the majority of studies have focused on the elderly. Those results show that "regular physical activity sustains cognition and delays the onset of dementia," van Praag says, and reduces "atrophy of gray matter volume and white matter lesions." A metastudy led by cognitive psychologist Arthur Kramer at the University of Illinois at Urbana shows that aerobic exercise particularly improves executive control function—the decision-making process, in essence—among old people. Just how much exercise is needed to get all these benefits has not been studied carefully yet, she says, "but preliminary observations indicate that unlimited voluntary exercise may be better for cognition in mice than a regime in which running is restricted to a few hours per day."

There's no denying that exercise is necessary for health, then, and that it makes you smart and happy to boot. But that still doesn't address the root of the question: How does exercise do all this? What are the mechanisms that connect a 10-mile run and, say, the failure of a mutant cell to run amok and form a tumor?



For now, there is only one grand unifying theory for how exercise does its magic. It invokes a phenomenon called hormesis. (I know, it sounds like an exotic massage therapy, but it's real biology.) Hormesis is a theory that attempts to explain why, in very small doses, toxic substances can actually have positive effects on health. For example, after imbibing trace amounts of the deadly poison dioxin, animals have a better chance of survival when exposed to a full dose. Shower animals in low doses of radiation, wait 24 hours, and then blast them with gamma rays. Those that were pre-exposed have a lower risk of dying of cancer. Hormesis in a nutshell: That which does not kill us makes us stronger.

The starting point for the hormetic theory of exercise is that intense physical activity is a source of toxins. By gushing oxygen through your system and accelerating your metabolism, you produce dangerous molecular by-products in your blood and tissues, especially free radicals, atoms with unpaired electrons that wreak havoc on DNA. So yes, exercise does damage the body even at the molecular level—but by exposing your body to small doses of these toxins through exercise, the theory goes, you stimulate a vast emergency network generating antioxidants to mop up free radicals, enzymes to repair broken DNA, and hormones to boost immunity. Exercise every day and hormesis keeps your body vigilant. Over the long term, that prevents disease.

Considering that the benefits of exercise occur throughout the body, in very different tissues and organs, "exercise fits well with the concept of hormesis," Zsolt Radák, a physiologist at Semmelweis University in Budapest, Hungary, tells me. Just like the dose-response curves for toxins, exercise follows "an inverted U-shaped" hormesis pattern: Low doses protect you from disease, but big doses—such as running consecutive marathons—are destructive. Still, the benefits of exercise "are much more complex than free radicals," Radák says.

The hormesis guru is Edward Calabrese, a toxicologist at the University of Massachusetts–Amherst. I ask him for evidence that hormesis is really what keeps runners a step ahead of disease. "The cell-based and in vitro studies of hormesis are consistent and convincing," he says, "but with living animals and people, the picture is rarely so clear." One problem is that the hormesis theory is disputed by prominent critics like Frederick vom Saal, a reproductive biologist at the University of Missouri at Columbia. (It is also often invoked to promote homeopathic medicine, thereby picking up the taint of pseudoscience.) But based on the evidence so far, "exercise is a self-administered drug that perfectly follows the hormetic curve," Calabrese says.

That sounds reasonable, but doesn't it seem bizarre that humans are designed to damage themselves in order to remain healthy? "It's a consequence of being a complex system with limited resources," Calabrese says. But then, I counter, why don't we have a physiology that functions equally well in active and sedentary lifestyles? "Evolution didn't design us that way," he replies.

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A more flexible physiology would surely be more complex, more metabolically expensive, and hence less efficient. Evolution cannot look forward to anticipate future behaviors. It could not have seen cars and couches on our horizon.

Radák has a different explanation. It is incorrect to think of exercise as a drug that people give themselves to boost health. Rather, lack of exercise—inactivity—is like a disease that causes health to decline. Doing things like running several miles every day "is just the normal way of living," he says.

I want to know if these scientists practice what they preach, so I question them about their lifestyles. "I manage to fit in about an hour of exercise a day," Cordain says with a sigh. "But sometimes I just spend so much time stuck behind this damned computer." Van Praag says her own research has "obligated" her to live an active life, "mainly long-distance bicycling" and one marathon so far. Calabrese is the über-athlete. At 60 years old, he still cycles two hours per day. "And I've kept a daily exercise journal since the age of 24," he tells me with equal parts pride and embarrassment. "I can tell you what exercise I did on the day we landed on the moon or when Reagan was shot."

They all applaud my year-round training regime—between one and three hours a day of running, swimming, biking, and weight lifting—but have mixed reactions when they find out how I manage it. For the past five years of my decade as an American expat in Europe, I've gone without health insurance. (I have only the minimum required accident insurance.) The money saved allows me to maintain my extravagant schedule of daily exercise, because it means I can put in less time working. Since exercise prevents the very diseases that health insurance covers, that trade-off strikes me as a logical one.

Cordain chuckles and asks, "How old are you?" I tell him I just turned 34. "If forced to choose between the two," he says, "I would side with you." The response of van Praag—who is my mirror image, having emigrated from the Netherlands to the United States—is as adorable as it is European. "Life is unpredictable, and everyone should have adequate, basic health insurance coverage," she says. "In your specific case, please make sure you wear a bicycle helmet, running shoes with reflectors, and sunscreen." Calabrese takes me by surprise. "I would choose the health insurance," he says. "I don't think exercise can make enough of a difference to offset the risk. Genes and chance are the major factors behind disease."

Calabrese's verdict gives me a sinking feeling. How much risk am I really offsetting with exercise? To find out, I consult one last expert. I-Min Lee is an epidemiologist at the Harvard School of Public Health. I ask her whether it would make sense to give up sports and work more so I could afford full health insurance.

"It depends," she hedges, "but first you should consider the evidence." The most comprehensive epidemiological data on exercise and health come from the Harvard Alumni Health Study, an ongoing survey of more than 21,000 men that started in the 1960s. "The general conclusion is the 'use it or lose it' principle," Lee says. "People with a physically active lifestyle are 30 percent to 50 percent less likely to develop cardiovascular diseases and cancers than similar people with inactive lives.

"Another major conclusion is that it's never too late to start exercising," Lee says. "Middle-aged men who change from being inactive to active," burning an extra 2,000 kilocalories per week, "are less likely to die prematurely than those who remain inactive." But there's bad news for me. Doing sports earlier in life doesn't make a measurable difference. "Those who exercise only in their college years and then stop have higher heart disease rates than men who do not exercise in college but take up physical activity in middle age," Lee says.

"So I'm not really earning extra years of life?" I ask. She may or may not hear my voice crack.

"No, you almost certainly are," she assures me. That is, unless I stop exercising for decades, which would erase all future health benefits. "The big risks for your age group are things like suicide and accidents," while the chance of getting heart disease "is hardly worth considering. Forty years old and onward, that's when the rates of major chronic diseases of the industrialized world start to increase exponentially."

"What would you do in my shoes?" I ask. I describe the varying responses from the other scientists.

"I'm in-between," she says. "The argument does make sense, but only because you are young. This strategy would not be wise after the age of 40."

So science has some pretty solid explanations of why exercise is good for you, and some quite solid numbers on how good it is for you. But as any reputable researcher can tell you, statistics reveal nothing about the individual. All I can do is start my next run, knowing that I'm doing my best to be the person evolution designed me to be. Ω