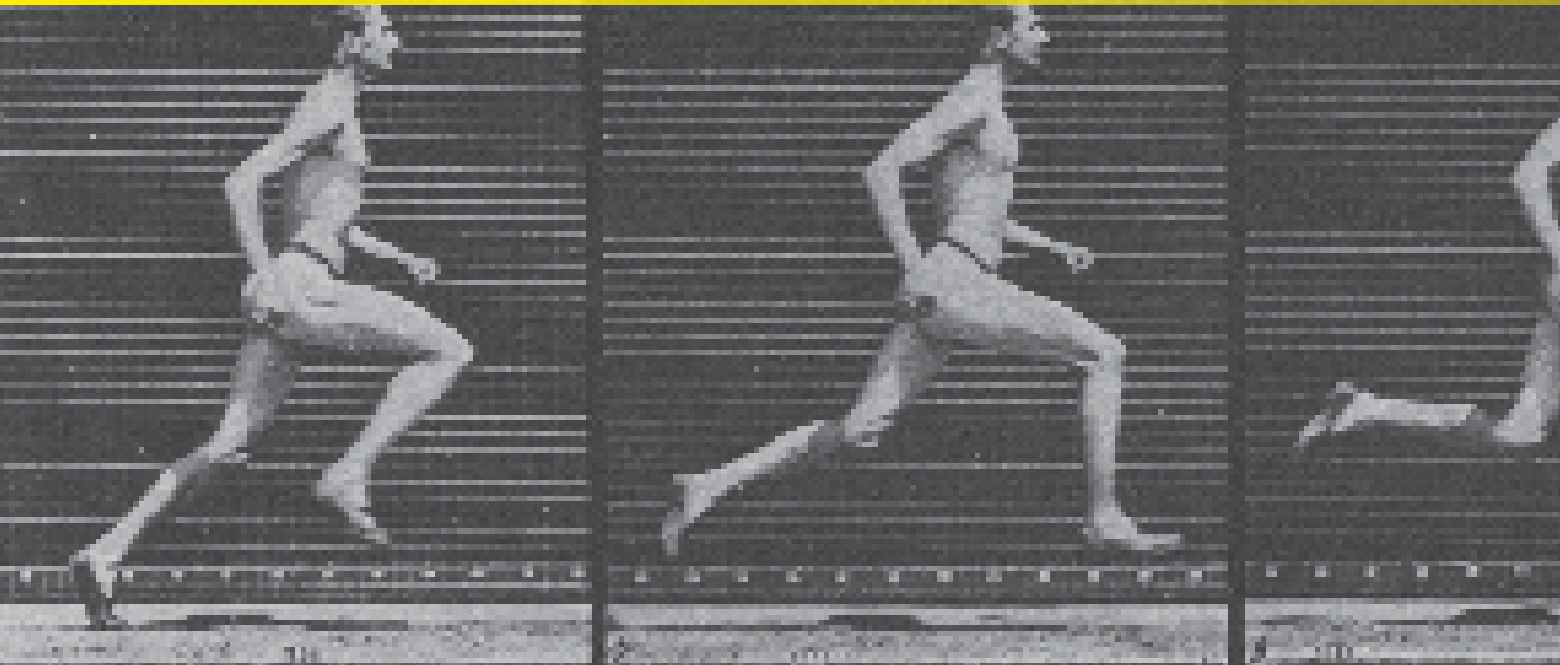


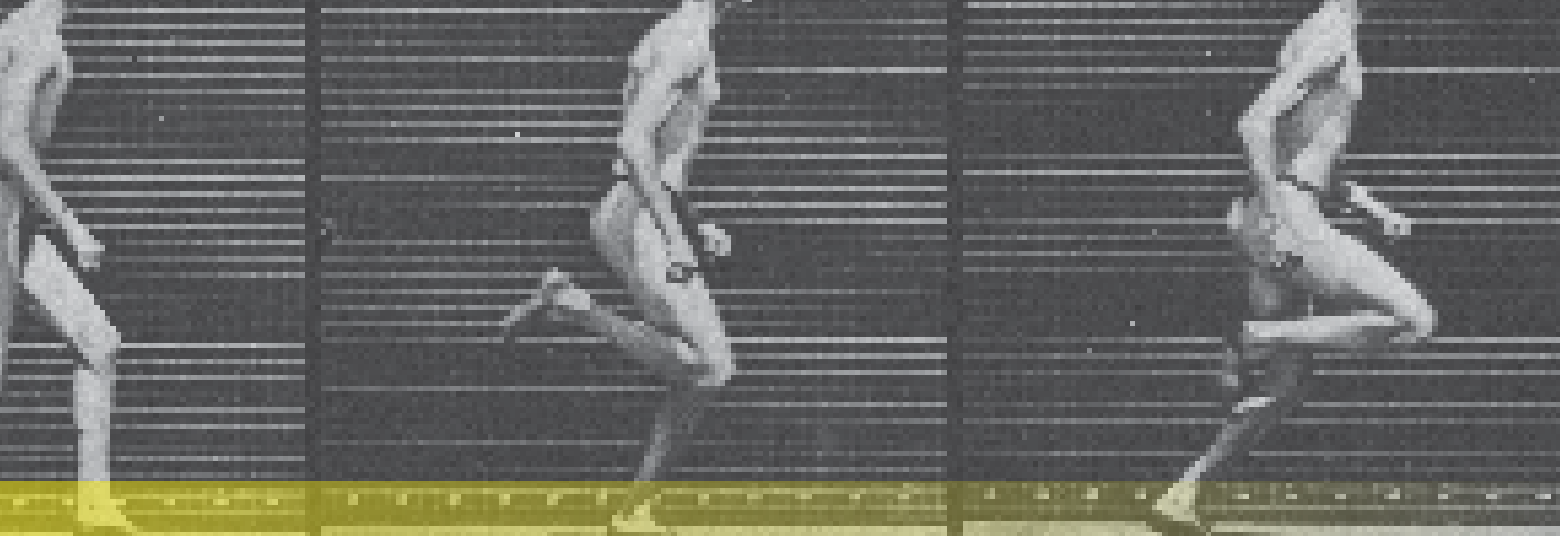
HEALTH

# WHY EXERCISE



First steps: In the 1800s Eadweard Muybridge perfected stop-motion photography to study human locomotion.

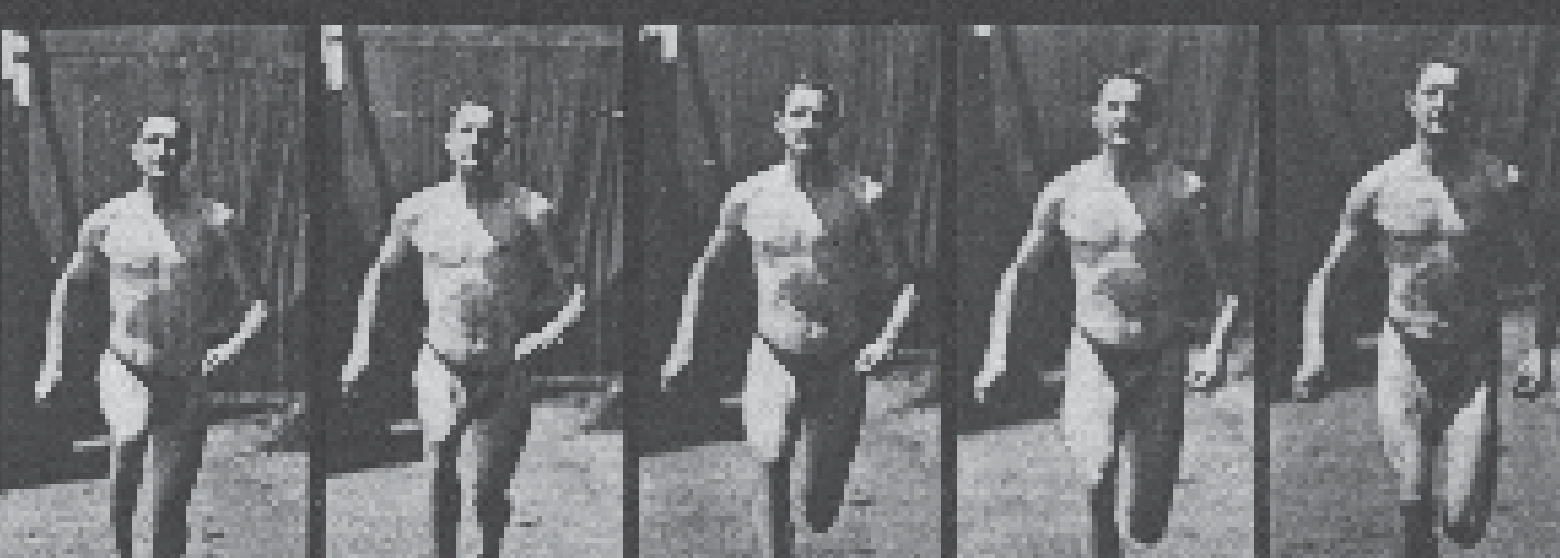
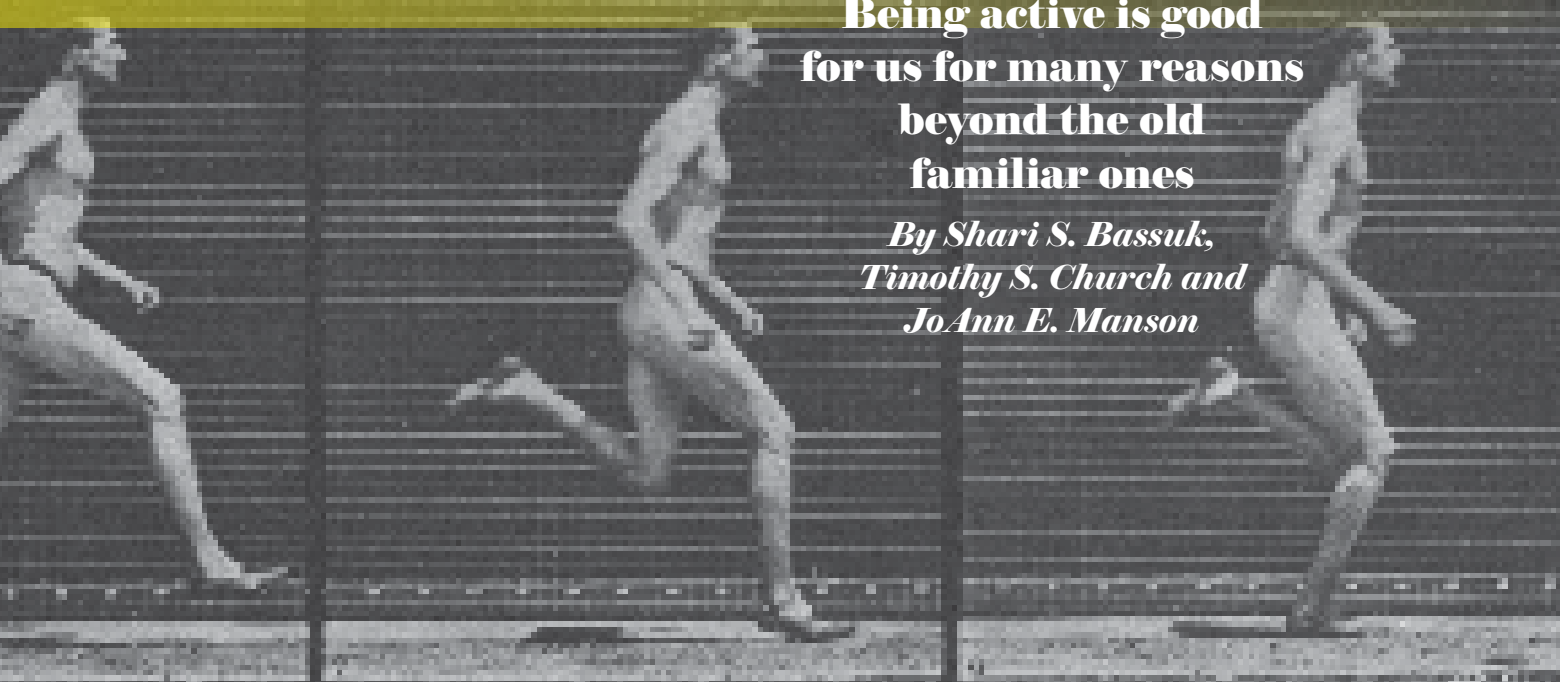




# WORKS MAGIC

**Being active is good  
for us for many reasons  
beyond the old  
familiar ones**

*By Shari S. Bassuk,  
Timothy S. Church and  
JoAnn E. Manson*



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**W**E ALL KNOW WE SHOULD EXERCISE. BUT FEW REALIZE THAT BEING PHYSICALLY active is the single most important thing that most of us can do to improve or maintain our health. Regular movement not only lowers the risk of developing or dying from heart disease, stroke and diabetes, it also prevents certain cancers, improves mood, builds bones, strengthens muscles, expands lung capacity, reduces the risk of falls and fractures, and helps to keep excess weight in check. And those are just some of the more familiar effects.

An explosion in research over the past few years has extended those observations even further. Among other things, exercise appears to boost brainpower—specifically the ability to carry out tasks that require attention, organization and planning, reduce symptoms of depression and anxiety in some people, and enhance the immune system’s ability to detect and fend off certain types of cancer. In addition, researchers are moving beyond describing the gross health benefits of regular physical movement to detailing the positive changes that occur at the level of cells and molecules for specific conditions such as atherosclerosis and diabetes.

Studies aimed at tracing the many ways, large and small, that various systems in the human body (cardiovascular, digestive, endocrine and nervous, to name just a few) are affected by exercise show that the benefits most likely result from minor to moderate improvements in many aspects of physiology, as opposed to large favorable effects on a small number of processes in particular cells and tissues.

Investigators have also come to realize that people need not be triathletes to reap exercise’s benefits. Twenty years ago preven-

tive health experts focused almost exclusively on the gains to be had from vigorous activity. Today they emphasize the value of sustained bouts of moderate movement as well. One of us (Manson) helped to demonstrate comparable benefits of moderate and vigorous exercise for several health outcomes in the large-scale Nurses’ Health Study and the Women’s Health Initiative. Based on data from these and other projects, the latest U.S. exercise guidelines (published in 2008) recommend the equivalent of at least 30 minutes of moderate activity, such as brisk walking, five or more days a week (or 75 minutes of vigorous activity, such as jogging, each week), plus 30 minutes of muscle-strengthening activity at least two days a week.

A closer look at some of the most exciting findings offers a taste of the less obvious ways that exercise protects our body and keeps it running well.

**IMMEDIATE EFFECTS**

TO FULLY GRASP the latest findings, it helps to know something about how the body generally responds to increased physical

**IN BRIEF**

<b>Routine physical activity</b> of moderate or vigorous intensity substantially reduces the risk of dying from heart disease, stroke, diabetes, cancer and other ills.	<b>Investigators</b> have recently identified numerous previously unknown ways in which habitual exercise can reduce the risk of heart disease and cancer, can	help control diabetes and can even facilitate learning. <b>Prolonged</b> sitting may, however, cancel some of the health advantages gained through regular exercise.
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## BEYOND THE HEART AND LUNGS

## Exercise Benefits Even Obscure Parts of the Body

Most people do not realize that sustained bouts of moderate to vigorous physical activity completely change our bodies from the inside out. Here is a look at a few of the less widely known effects, starting with the neural connections in the brain and extending all the way out to the major muscles and bones of the limbs.

### Nervous System

Exercise improves cognitive function. Aerobic training helps older adults in particular with organization, planning and attention.

### Immune System

Regular physical activity protects the body from inflammation; however, too much exercise can weaken the immune system's ability to fight off germs.

### Musculoskeletal System

Weight-bearing exercise and balancing routines help to prevent fractures and falls. Aerobic fitness decreases everyday fatigue by increasing muscular efficiency.

### Genetics

Scientists are identifying the specific genes that get turned on or off by changes in physical activity. The effects are usually modest, but they occur across a wide range of cells.

### Endocrine System

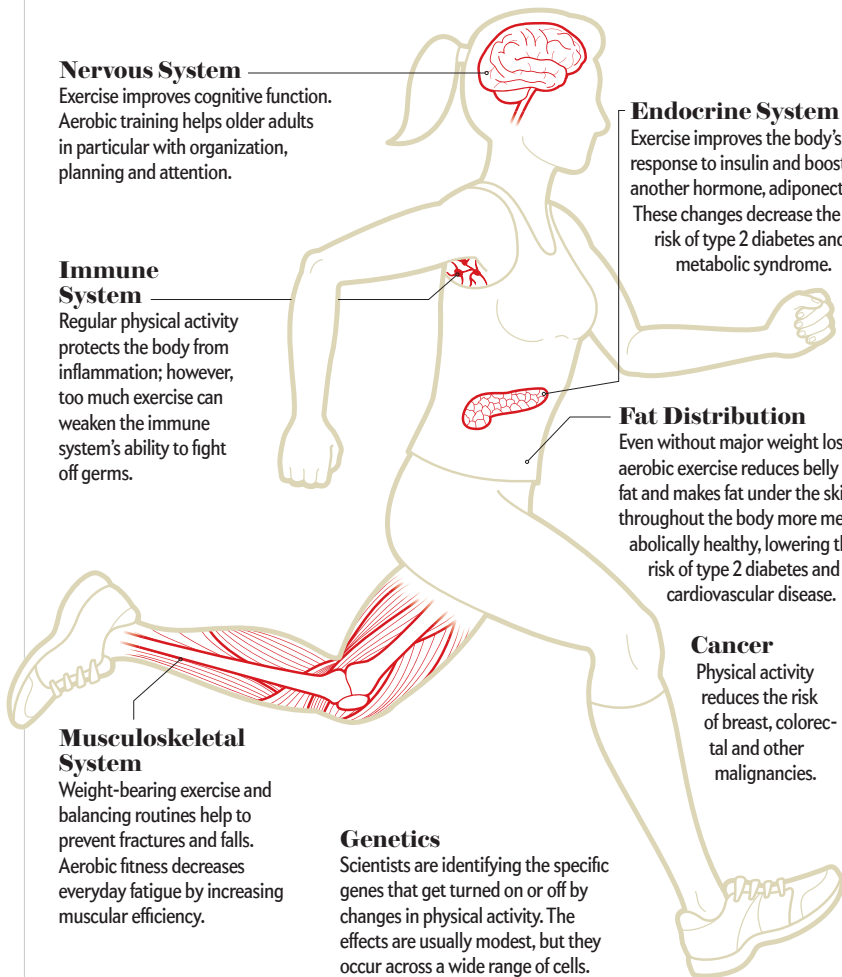
Exercise improves the body's response to insulin and boosts another hormone, adiponectin. These changes decrease the risk of type 2 diabetes and metabolic syndrome.

### Fat Distribution

Even without major weight loss, aerobic exercise reduces belly fat and makes fat under the skin throughout the body more metabolically healthy, lowering the risk of type 2 diabetes and cardiovascular disease.

### Cancer

Physical activity reduces the risk of breast, colorectal and other malignancies.



level if you can talk or recite a poem while you are moving. If you can croak out only a word or two at a time, then you are exercising vigorously. At the other end of the scale, if you can sing while moving, then you are working at a light level of intensity.

Whenever a person picks up the pace, the nervous system prepares all the body's organs for action. Initially the individual may notice a heightened sense of awareness, increased heart rate, quickened breathing and light sweating. Internally, blood flow is reduced to those organs, such as the gastrointestinal tract and kidneys, that are not essential for movement. At the same time, blood vessels in the active muscles open up, ensuring that enough oxygen-rich blood flows to those muscles that are working the most.

Once in the muscle cells, oxygen diffuses into cellular structures called mitochondria, which use it to generate energy for the cell. The basic fuel for this process is the sugar molecule glucose, which the body creates through the breakdown of larger food particles and absorbs during the course of digestion. The addition of oxygen to glucose in mitochondria triggers a highly efficient kind of combustion. When oxygen is available, mitochondria can create nearly 20 times more energy per glucose molecule than they can in the absence of oxygen.

The body first burns up glucose molecules that are stored in the form of a compound called glycogen, found primarily in the liver and muscles. But as exercise continues, the available stock of glycogen is depleted and molecules of triglyceride (which is a kind of fat) become the chief source of fuel. All this internal combustion produces certain by-products, such as lactic acid and carbon dioxide, which seep from the muscles

demands. Exercise means different things to different people. From snowshoeing to swimming to a fast walk on the beach, exercise can take many forms and occur at differing levels of intensity. Aerobic exercise is the type that significantly boosts the amount of oxygen needed by the muscles, requiring the lungs to work harder. Its health benefits are also the best understood. But more stationary forms of exercise—such as lifting weights or practicing one's balance—also have their place.

Scientists have developed fairly rigorous methods for measuring the intensity of aerobic exercise in research laboratories. An effective and much less expensive way to measure how much you are pushing your body outside the lab is the talk test. Moderate activity begins when your heart starts beating faster and you are breathing more heavily. You are still at a moderate

into the bloodstream, where they are sensed by the rest of the body. The increasing concentration of these wastes prompts further biochemical reactions in the brain, lungs and heart that eventually make removal of these compounds more efficient and less tiring.

The benefits of exercise really start to accumulate once physical activity becomes a routine habit. The body adapts to the increasing demands being placed on it, leading to increased stamina as individuals become more fit. For instance, the lungs process more oxygen as each breath becomes deeper and the heart pumps more blood with each beat. These adaptations, which typically begin to show up within a few weeks of meeting or exceeding the federal guidelines on physical activity, also lead to changes in biology that improve long-term health.

## MOLECULAR CHANGES

ENTIRE LIBRARIES could be packed with data demonstrating the effects of exercise on everything from major organ systems to how various genes are turned on or off. A few top-level conclusions are outlined in the infographic that accompanies this article [*see box on preceding page*]. But we will focus here on some of the newly discovered mechanisms that help to explain why exercise expands our cognitive capacities, improves our ability to control blood glucose levels and strengthens our cardiovascular system. These changes have a greater effect on the quality of daily life than almost any other exercise benefits.

Athletes have long known that exercise boosts their mood and mental health. And yet it was not until 2008 that scientists were able to directly measure the so-called runner's high—a sense of euphoria that occurs after prolonged exercise. Not only did they show that the brain released more endorphins (opioidlike hormones that evoke pleasurable feelings) during a long-distance run, they also determined that the compounds were active in regions of the brain responsible for strong emotions. (Previous work had detected an endorphin surge only in the bloodstream, which was unrelated to changes in the brain.)

More recently, investigators have focused on the chemical changes in the brain by which exercise enhances our ability to concentrate, think and make decisions. In 2011 a scientifically rigorous experiment—known as a randomized controlled trial—of 120 people in their 60s and 70s demonstrated that exercise increases the size of a part of the brain called the hippocampus. The study's authors noted that the specific portion of the hippocampus that was affected by exercise is one that allows people to remember familiar surroundings; it is also one of the few areas of the brain that makes new nerve cells—at least in rats. Newborn neurons are thought to help with distinguishing similar but different events and things. Animal studies have further shown that exercise increases the levels of the chemical responsible for triggering the growth of these new neurons—a molecule known as brain-derived neurotrophic factor, or BDNF. Most recently, animal studies have identified a protein produced in the hippocampus that is responsible for increasing BDNF expression and turning on genes related to cognition. Researchers are hoping to develop an injectable form of this protein, called irisin, that could eventually be used to boost brain-protecting pathways.

Now research is challenging what we thought we knew about how exercise prevents heart disease. Scientists initially believed that routine activity reduced cardiovascular risk largely by decreasing blood pressure and lowering the amount of LDL cholesterol (also known as the bad cholesterol) while raising the amount of HDL cholesterol (the good cholesterol) in the blood. This conclusion was only partly correct. Exercise does in fact lower blood pressure substantially for some individuals, but for most people this benefit of exercise is relatively small. Moreover, exercise—particularly resistance exercise, such as weight training—can raise HDL cholesterol, a change that typically takes sev-

eral months to emerge, although the effect is fairly modest—on the order of a few percentage points.

Further investigation has shown that the more important LDL-related effect has to do with how exercise changes the molecule's properties as opposed to reducing the amount found in the blood. Technically speaking, LDL is not synonymous with cholesterol; rather it carries cholesterol through the bloodstream the way a delivery truck carries groceries. (Being made of fat, cholesterol cannot dissolve in the watery environment of the bloodstream, so it has to be packaged in something that can.) LDL particles also come in various sizes in the same way that groceries can be delivered in minivans or giant trucks.

Over the past several years a growing number of scientists have found that smaller LDL molecules are particularly dangerous. They have a tendency, for example, to lose electrons, which then ricochet around the blood vessels damaging other molecules and cells (think crazed driver behind the wheel of a beat-up van). Large LDL molecules, on the other hand, are much more stable and float through the bloodstream without crashing into anything (more akin to big, well-maintained trucks with professional drivers).

Studies now show that exercise increases the number of larger, safer LDL molecules while decreasing the number of small, dangerous ones, and it alters the ratio by boosting the activity of an enzyme called lipoprotein lipase in fat and muscle tissue. Two people with the same amount of cholesterol in their blood but different levels of physical activity could thus have very different risk profiles for cardiac disease. The couch potato would probably have a lot of small LDLs and very few if any large ones, whereas large

LDL molecules would predominate in the active person's blood. And yet despite having an identical cholesterol level, the first person would have several times the risk of suffering a heart attack of the second person.

Regular physical activity positively affects another key component of the blood—the sugar glucose. The liver, pancreas and skeletal muscles normally work together seamlessly to make sure that each part of the body gets the sugar it needs, whether you are at rest or active. By definition, exercise places increased demands on the skeletal muscles, which need increasing amounts of glucose to fuel their efforts. Over the long term, exercise also prompts the fibers within the muscle to become more efficient at using glucose, making the muscle stronger.

The liver responds immediately to the call for more fuel by churning sugar molecules into the bloodstream, and the pancreas releases a hormone called insulin that signals the cells to draw increasing amounts of glucose out of the blood. You might imagine that the whole process could lead to wild swings in glucose levels, but the body works hard to keep its blood sugar levels within a fairly limited range of between 70 and about 140 milligrams per deciliter (and well below 126 mg/dL in the fasting state)—at least in folks without diabetes. One reason that blood sugar needs to stay above 70 mg/dL is that the brain depends heavily on glucose as its primary source of fuel and thus is acutely sensitive to any change in the amount found in the blood. Although extremely

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low glucose levels can lead to coma and death in a matter of minutes, it is just as important not to spend long periods at the high end of the scale. Broadly speaking, extra sugar in the blood tends to gum up the works, causing cells to age prematurely.

As exercise becomes more of a daily habit, the muscles grow more sensitive to the effects of insulin. That means the pancreas does not have to work as hard to help keep glucose levels in check; lower levels of insulin will accomplish the same result as higher amounts once did. Doing more with less insulin is particularly helpful for people with type 2 diabetes, whose bodies have trouble keeping blood sugar in the normal range, in large part because they have become resistant to the hormone's effects. But insulin also promotes the proliferation, or rapid production, of new cells—and as such, elevated levels have been linked to a greater risk for developing breast and colon cancer in particular.

Recently physical activity has also been shown to promote the uptake of glucose through another pathway that does not require the presence of insulin. Having a second pathway to get glucose out of the bloodstream and into the muscle cells could open up new directions in the treatment of diabetes.

Intriguingly, the greatest benefits for people with diabetes seem to come from mixing different types of exercise. Two large randomized clinical trials have reported the combination of aerobic and resistance exercise is better at controlling blood glucose levels than either type of exercise alone. The first study was conducted in such a way, however, that it was unclear if the benefit came from the combination of exercise types or the fact that participants who underwent aerobic and resistance training also ended up exercising longer than their counterparts who followed a single exercise program. One of us (Church) decided to tackle that question by leading a second trial in which 262 previously sedentary men and women with diabetes were divided into four groups: an aerobic exercise group (who walked on a treadmill), a resistance group (seated rowing, leg presses, and the like), a combination group, and the control group, which undertook weekly stretching and relaxation classes.

Each of the groups who engaged in physical activity expended the same amount of time and effort (approximately 140 minutes per week) over the course of nine months. They also all lost inches off their waist, and both groups that performed aerobic exercise became more fit. But only the group that undertook both resistance and aerobic exercises exhibited a significant drop in their blood in the amount of a protein called HbA1c, which acts as an indicator of average blood sugar level over the past several months. The additive benefit suggests that aerobic and resistance training operate through different physiological mechanisms—an idea that investigators are actively pursuing.

Another way that continued exercise strengthens muscles is by boosting the formation of energy-producing mitochondria. In response to regular exercise, muscle cells start making a protein called PGC-1 $\alpha$ , which directs the cells to churn out new mitochondria. More mitochondria mean each cell can convert more glucose into energy.

### SITTING HAZARD

GIVEN THE MULTIPLE health benefits of moderate exercise, you might expect that everyone is lacing up their walking shoes and heading out the door. But many Americans fail to achieve even the recommended half an hour of moderate activity on five or

more days of the week. Only 52 percent of U.S. adults are active enough to meet the aerobic exercise guideline, and 29 percent strengthen their muscles as recommended twice a week for 30 minutes at a time. One in five Americans meets the recommendations for both aerobic and resistance exercise.

The difficulties of changing people's sedentary habits have prompted scientists to investigate whether lighter or shorter bouts of exercise have any health benefits. Positive results, they hope, might motivate even couch potatoes to start moving more than they are used to doing. So far the data suggest that even minimal daily exercise routines can extend people's lives somewhat. A 2012 analysis of the data from six studies, totaling 655,000 adults in the U.S. who were tracked for about 10 years, found that people who expended as little as 11 minutes per day on leisurely activities (gardening, washing the car, taking an evening stroll) had a 1.8-year longer life expectancy after age 40 compared with their inactive peers. Admittedly, participants who met recommended guidelines for moderate activity were better off; their life expectancy was 3.4 years longer. And those who were active between 60 and 90 minutes each day achieved even greater gains (4.2 years longer life expectancy).

Despite the advantages of minimal efforts, a comprehensive look at exercise studies to date shows that most people would benefit from ramping up their activity—for example, adding moderate activity if they are light exercisers or short bursts of vigorous activity if they are moderate exercisers. Perhaps the worst news for today's office-bound knowledge workers is that sitting for more than six hours a day during leisure time may prove harmful even if you also manage a few high-intensity workouts. Still unknown: whether it is something about sitting itself that is a problem or the lack of movement usually associated with it.

Given the continual and growing evidence for the health benefits of physical activity, the message is clear. Regular prolonged movement—at whatever intensity level can be safely managed—needs to be built into everyone's daily habits and physical environments. It should become as easy as jumping into a car is now.

We strongly recommend that doctors and other health care providers regularly write a prescription for exercise during routine office visits. In addition, we advocate for increased research into the kinds of behavioral programs, public health campaigns and changes in urban design that will facilitate sustained levels of beneficial physical activity in our largely sedentary society. ■

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#### MORE TO EXPLORE

**Global Recommendations on Physical Activity for Health.** World Health Organization, 2010. [http://whqlibdoc.who.int/publications/2010/9789241599979\\_eng.pdf](http://whqlibdoc.who.int/publications/2010/9789241599979_eng.pdf)  
Physical Activity Guidelines for Americans: [www.health.gov/paguidelines](http://www.health.gov/paguidelines)

[scientificamerican.com/magazine/sa](http://scientificamerican.com/magazine/sa)