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Survival of the unfit

Understanding biology of prehistoric ancestors sheds light on modern chronic maladies

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The prehistoric hunters ran for miles in blazing heat across grassy plains chasing antelope. When the animals rested, the men shouted and leapt, frightening the exhausted creatures to flee again, and again. By mid afternoon, one antelope, its mouth agape and drooling, was so weak it could run no more. The men speared it to death.

For hundreds of thousands of years, our ancient ancestors took prey in this manner, known as persistence hunting. Their fine-tuned bodies — cooled by sweat — allowed them to walk, run and sprint for hours in the African sun.

The genes and hormones they carried, we carry in us. Their biology is our biology.

But something has gone terribly wrong. Science may know why.



Modern sedentary life has damaged humankind's inherited biological system built for exercise,

In recent years, researchers at the University of Missouri and other institutions have taken a new approach to the fattening of America, where nearly half are overweight and one-third obese. Rather than explore environmental factors, scientists are studying the science behind inactivity, aerobic exercise and weight gain. Ground zero for researchers is the physiology of hunter-gatherers, some of whom still exhaust their prey on the African savannah.

Prehistoric humans were incredibly fit compared to people of modern times. Today's conveniences have created a sedentary society that has degraded an inherited biological system built for aerobic exercise. Consequently, inactive people are at risk for chronic health maladies such as coronary heart disease, various cancers, type 2 diabetes, hypertension and obesity.

What can be done? The answer might sound like a cliché: Eat better and exercise.

Mizzou researchers want to tweak the cliché just a bit. They understand the benefits of healthful eating, and if Americans can eat smart and be active, great. But they also realize most diets fail, and people are lazy about exercise. At least one MU study suggests that being overweight and active may be healthier than being normal weight and inactive.

“Don't worry about weight. Get active,” says Tom Thomas, professor emeritus of exercise physiology. “You can be fit but fat.”

Stone age genes

The physical conditioning of hunter-gatherers was similar to that of today's distance runners, says Frank Booth, professor of biomedical sciences. If you were to strap a pedometer on a prehistoric man, it would read between 13,000 and 20,000 walking steps a day, Booth says, which is approximately 5 to 8 miles. Women might walk some 11,000 daily steps to gather food and perform other duties. Most Americans today, by contrast, are taking 2,000 to 5,000 steps, about a four-fold reduction in activity for men and three-fold reduction for women.

What's best: Walking, biking or running?

Exercise newbies often are saddled with deciding what aerobic exercise to take up.

On the short list are walking, biking and running. Each comes with its own advantages and disadvantages.

Walking may be easiest on the body but, depending on how far you walk, generally offers less metabolic benefit than biking and running. That's not to say walking isn't beneficial. Studies show that walking as little as 30 minutes a day reduces the risk of many chronic health maladies.

For people who have not exercised in a long time, walking has become a popular gateway exercise to get the blood circulating and the muscles moving. From there, brisk walking is a common next step, said John Thyfault, MU associate professor of nutrition, exercise physiology and internal medicine.

Biking, another popular aerobic exercise that's easy on the body, also improves health. Stationary bikes are a great option for people who don't

Our genetic heritage was refined through natural selection to favor movement. “If you were not physically active, you starved and died,” Booth says. “Those who moved the most efficiently would pass on their genes. The human body is not designed for physical inactivity. This has contributed to the health problems facing sedentary modern societies.”

During a February 2012 lecture in MU’s Tate Hall, Booth, who’s thin as a rail, talked about a Copenhagen experiment analyzed by him and John Thyfault, associate professor of nutrition, exercise physiology and internal medicine. The volunteers were 10 fit young men who averaged 10,000 steps a day. Their activity was reduced to 1,500 daily steps, an 85 percent decrease in exercise. Rather than climbing stairs, the men took elevators. Rather than walking, they drove.

In other words, they mimicked everyday life for many Americans.

After 14 days, the men had increased body fat by an average of 7 percent. Their insulin sensitivity — a prelude to insulin resistance, itself a harbinger of type 2 diabetes — was negatively altered, and their muscle mass had decreased.

If a reduction in health can happen so fast to young active adults, what must it do to people who live for decades this way?

“Epidemiological evidence suggests that individuals at the higher range of [pedometer] activity better protect themselves from chronic disease risk,” Thyfault co-wrote in June 2011 for the *Journal of Applied Physiology*.

The "thrifty gene"

To understand the unhealthful effects of inactivity, scientists expand on the “thrifty gene” idea first set forth in 1962 by geneticist James V. Neel. Thrifty gene scholarship combines studies in genetics, hormones and lifestyle in one Darwinian swoop.

The idea is that prehistoric humans who were

want rain, sleet, snow and honking autos to interrupt their workout.

The downside of biking is that only the hip and leg muscles are typically used, so it’s not a whole-body workout. Pam Hinton, MU associate professor of nutrition and exercise physiology, has conducted studies showing that bone density is weaker in regular cyclists than in regular runners. Cyclists showed more signs than runners of osteopenia, a low-bone density condition that can lead to osteoporosis. Weakened bones means more susceptibility to fractures.

However, by combining strengthening exercises like fast aerobics or weightlifting, bikers work more muscles and decrease the chance of developing osteopenia, researchers say.

Running is the hardest on the body, especially the knees, but offers the best workout of the three. Progressing from brisk walking to jogging to running is something many doctors recommend. As with walking, running can be done on a treadmill for those who prefer their exercise at home or in a gym.

A runner since the 1960s, Frank Booth, professor of biomedical sciences, says varying speed by walking then jogging then running then walking again is healthful and avoids overstressing the body.

“Choose something you enjoy and that fits into your

biologically efficient, or thrifty, in processing food had an evolutionary survival advantage. Since there were no Jimmy John's around the corner, ancient people expended enormous energy finding food. A successful hunt or food-gathering stint allowed for the "thrifty" storage of energy in muscle and fat that the body could retrieve when food was scarce.

schedule," Booth says of the aerobic triune. "This is something you will be doing for 50 years. The most important thing is to stay active or else your body will disintegrate."

Aiding food storage was the so-called fat gene, or FTO, that helped carriers store fat when they were inactive. The gene, discovered by scientists in 2007, gave carriers an edge in surviving short famines, which made it more likely they'd pass their genes on to offspring.



Booth and other scientists offer a refinement of thrifty gene scholarship that explains how inactivity may foster chronic health problems.

Years of reviewing medical records and conducting controlled experiments with lab rodents and humans suggest that aerobic exercise helps explain the thrifty gene process. Blood glucose, the body's main energy source, enters muscles being physiologically stressed, with a little help from the hormone insulin. But when a person is inactive for long periods, the thrifty gene process malfunctions.

Insulin is forced to work extra hard to transport glucose from blood to muscle. To pull it off, the pancreas produces more insulin, which can lead to insulin sensitivity, as shown in the 2011 Copenhagen study. Meanwhile, glucose accumulates as fat.

The process was well fitted to our prehistoric ancestors, Booth and Thyfault say. After a brief famine, resumption of activity exercised muscles, which triggered the return of glucose and insulin to their normal tasks. But for modern sedentary people, the aerobic trigger is missing. Like water in a knotted hose, glucose and insulin build up to unhealthy levels in the blood that can lead to chronic ailments.

What would happen if these inactive people were carrying a fat gene? This is not far-fetched. FTO is believed to be in more than 60 percent of those of European and African descent, and

nearly half of those of Asian descent. By some estimates, the gene increases by more than 10 percent a sedentary carrier's propensity to be overweight or obese, Booth says.

Once a blessing, the FTO gene and its variants today might be a curse. "The same genes that were selected for survival when people had to forage for their food may now shorten survival in the absence of sufficient physical activity," Booth says.

Crash diets crash

Thrifty gene scholarship also helps explain the failure of most crash diets, researchers say.

When people lose more than 10 percent or 15 percent of their weight, the body thinks it's starving on the ancient African savannah and becomes stingy with its energy. The body in survival mode undergoes a variety of metabolic and hormonal changes. The result is that struggling dieters experience strong food cravings and gain lost weight back.

Susan Washington, a 51-year-old customer service representative in Printing Services at Mizzou, has struggled with her weight for most of her adult life. Washington said she's tried many diets, but her weight always returned to about 170 pounds.

"I'd get food cravings," she says, "and they'd come back stronger and stronger. I couldn't stay with it."

In reaction to dieting, the body increases appetite through hormone activity and conserves energy by slowing metabolism during light exercise by as much as 25 percent, Booth says. After losing weight, dieters are burning fewer calories than people who maintain that weight normally. A dieter might need only 2,300 calories per day to maintain the target weight, while someone naturally at that weight could chomp down 2,700 calories a day.

Next time you hear crash dieters insist they eat as much as a thin person and still gain weight, believe them. The body defends the higher weight for years, perhaps decades.

Success through sweat

Given the body's fight against weight loss, it may seem that the chronically overweight are out of luck. But scientists say there is hope, though perhaps only for those willing to sweat.

In August 2011, Washington decided to have another go at weight loss. She bought a treadmill and walked on it 60 to 90 minutes every day, and she ate in moderation. Because her two children were now away at college, Washington had more time to manage her weight. She also received support from Healthy for Life, a University of Missouri System wellness program for faculty and staff.

By October she was down to 150 pounds, a 10 percent reduction. By winter she was at 125 pounds, and she has maintained that weight.

It has taken tremendous effort. Her life is centered on food management, outdoor activity and treadmill workouts. "You have to organize your life around exercise and eating right," Washington said.

But most people don't have the time, the will or, perhaps, the genes to lose weight and keep it off. For them, the solution may be adopting a realistic view of dieting. Thyfault recommends a maximum 5 percent to 10 percent weight loss to embattled dieters. This amount improves health and reduces risk of metabolism-related maladies, he said.

Researcher Thomas goes even further. Exercise? You bet. Diet? Let's talk.

In a controlled experiment by Thomas and others published in the July 2010 *Journal of Applied Physiology*, 102 overweight and obese adults went on a program of diet and aerobic exercise until they lost 10 percent of their weight. Next, researchers had the volunteers regain all of the weight back — half while performing aerobic exercises and the other half ceasing exercise altogether. Thomas found that the exercisers generally maintained their improvements in metabolic health. The non-exercisers did not.




Moral: Exercise may trump diet when it comes to better health.

It might also inhibit the fat gene from being expressed. A November 2011 report in *PLoS Medicine* found that patients who performed as little as one hour of moderate to intense activity a week subverted the gene by 30 percent.

Plenty of questions remain for future studies of the relationship between the fat gene and exercise, and physiology and weight gain. But for Thomas, one thing is certain: "There is less chance for weight maintenance without exercise."

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