

Are some people doomed to be fat?

by Linda Geddes

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Some people can't lose weight – and others can't put it on. What separates whippets from walruses?



MY HUSBAND is the kind of man that most people hate. He can eat three helpings of dinner, yet stays steadfastly slender. He plays football just once a week, but throw him into a half marathon and he will complete the entire course in a faster time than most of those who have slogged through weeks of training. He once had a full body scan and was told they had never seen someone with so little internal or surface body fat. He doesn't, to my knowledge, have worms.

We all know people who eat like horses yet are as skinny as rakes, while others, like me, seem to pile on the pounds just thinking about food. At the heart of the difference is metabolism, the sum of the chemical reactions occurring in the body at any given time. Clearly there is more to it than a simple balance between calories eaten and calories burned through exercise. But many of our popular conceptions about metabolism don't stand up to scrutiny. So what is the difference between people like my husband and those like

me? And can we use that knowledge to take our metabolic fates into our own hands?

It was the 17th-century physician Santorio Sanctorius who launched the study of metabolism. For three decades, he used a specially constructed "weighing chair" to record his weight before and after eating, sleeping, working, sex and excreting. He also weighed the food and drink he consumed and his waste products. Through these rigorous – and at times messy – studies he discovered that for every 3.6 kilograms of food consumed, he excreted just 1.4 kilograms of waste. The rest, he concluded, was lost through his skin as "insensible perspiration".

We now know that the fats, carbohydrates, proteins and alcohol we consume enter our cells and are fed into a complex network of biochemical pathways, eventually generating energy. Any excess is channelled into one of two energy stores: glycogen in the liver and muscle and, when that store is full, fat.

The central regulator of metabolism is the thyroid gland, a butterfly-shaped organ that sits at the front of the neck and releases hormones that speed up the rate at which cells generate energy. "If your thyroid gland is overactive you'll become very hot and eat a massive amount but be as thin as a rake," says Steve Bloom, head of the division for diabetes, endocrinology and metabolism at Imperial College London. An underactive thyroid, on the other hand, causes people to become cold and clammy and lose their appetite but gain weight all the same. Both conditions only affect around 1 in 1000 men. Women are more prone, with around 1 in 100 having an overactive thyroid and 15 in 1000 affected by an underactive thyroid. "Metabolic rate can certainly control body size," says Bloom. "The problem is that people will extrapolate and claim: 'I've got a metabolic defect; that's why I'm fat.'" Conversely, my husband maintains that the reason he is so thin is that he has a fast metabolism. It's probably not that simple.

Idling takes energy

You can measure a person's resting metabolic rate by putting them into a metabolic chamber, a small room where they live for a period of time, typically 24 hours. During this time, the amount of heat they release, the oxygen they consume, the carbon dioxide they produce and the nitrogen they

excrete are carefully measured to calculate their total energy expenditure. Comparing obese and thin people in this way has produced some surprises. "If you measure an obese person at rest and a lean person at rest, the obese person will actually be expending more calories," says David Stensel at Loughborough University, UK. What is going on?

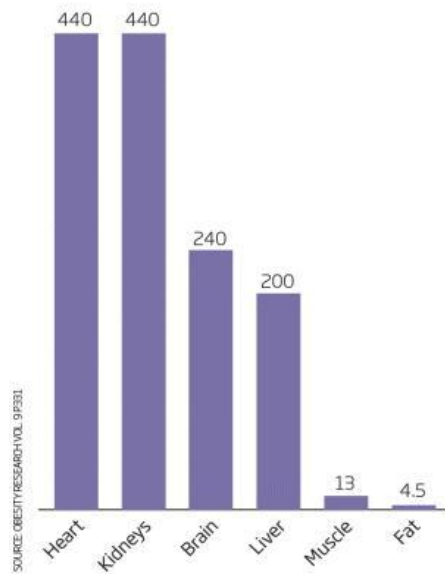
For a start, larger people have more cells to keep going. But it's not just the number of cells you maintain; the type matters too. Muscle cells burn calories around three times faster than fat cells, but they are far from being the most energy-hungry; while you rest, 1 kilogram of muscle burns just 13 calories a day, whereas 1 kilogram of heart or kidney tissue burns 440 calories (see diagram). "Although obese people have more fat, they have also got a greater fat-free mass and they tend to have larger organs," says Stensel.

This is bad news for anyone hoping to boost their metabolic rate by building muscle? Substituting 1 kilogram of fat for 1 kilogram of muscle means you will need around 9 calories extra per day – hardly *carte blanche* to eat whatever you choose. Still, having a relatively greater proportion of muscle to fat does go some way to explaining why men need more calories on average each day than women. It also partly explains why people's energy requirements drop slightly as they age (see diagram). The average 20-year-old man, for instance, has some 5 kilograms more muscle than the average 60-year-old man.

Busy body parts

Some of your organs need far more energy to keep them ticking over than others

Resting metabolic rate (kcal/kg/d)



What you eat and when you eat it can make a difference to the weight you gain

Of course, resting metabolic rate isn't everything – the more active you are, the more calories you burn. However, my husband's weekly football session doesn't seem to cut it, and there are plenty of skinny people who swear they never exercise. What's their secret?

One possibility is that they are more active than they realise. James Levine at the Mayo Clinic in Rochester, Minnesota, recruited 20 self-proclaimed "couch potatoes", some slender, some mildly obese. All were fitted with sensors to monitor their posture and movements over 10

days. Even though none of them did any exercise as such, the mildly obese couch potatoes sat for 2.5 hours longer each day than the lean ones – equivalent to a difference of 350 calories per day. "That's more than enough to explain how someone gains weight over time," says Stensel.

And we shouldn't dismiss the notion that some people are just naturally more inclined to gain weight than others. Claude Bouchard at the Pennington Biomedical Research Center in Baton Rouge, Louisiana, recruited 12 pairs of identical male twins who were prepared to pile on the pounds for the sake of science. For two weeks they ate normally while Bouchard calculated how many calories they needed each day to maintain their weight. Then he overfed them by 1000 calories a day, six days a week for 14 weeks – equivalent to 84,000 excess calories per person overall.

Within twin pairs, weight gain tended to be very similar, but there was a three-fold variation between the different sets of twins. "It ranged from about 4 kilograms to 12 kilograms," Bouchard says. A follow-up study with other twins showed a similar pattern in variation in the amount of

weight lost in response to exercise. Such studies strongly hint that genetic factors control our propensity to gain weight. But how?

Over the past two decades, Bouchard and his colleagues have been trying to tease out some answers. They have so far identified five factors that consistently predict greater weight gain: low muscle mass, low overall fitness, low levels of testosterone (which stimulates muscle growth), being less responsive to the fullness hormone leptin, and burning less fat in the diet directly as fuel. "None of them is the golden bullet," says Bouchard, although we do have some control over some of them.

What's your fuel mix?

I am particularly intrigued by the last. It suggests that if my husband and I were to eat identical large meals, my body cells would predominantly generate energy from glucose (from the digestion of carbohydrates), whereas his would use more of the fats in the food. Having eaten more calories than we immediately needed, we would both store the excess.

However, he would burn more calories doing this as he would be left with more glucose circulating in his blood than me, and excess glucose must be converted to fat for storage, a process that expends energy. "We are only talking about small differences in the fuel mix that people use," says Bouchard, "but these could make a substantial difference to their propensity to gain fatty tissue."

This suggests that some people's bodies are simply better at dealing with excess food without putting on weight. It's an idea that finds favour with Daniel Bessesen at the University of Denver in Colorado. His studies show that "obesity-resistant" people respond to overfeeding by burning more fat than "obesity-prone" people – while they are sleeping. Understanding the role of sleep in weight gain is still in its infancy. "Sleep is an important time where your brain assimilates information from the day in terms of memories, but I wonder if that's true of nutrient metabolism as well," he says. "The brain has to decide 'how much did I eat today?' and then burn those calories or adjust the food intake for the next day."

Bessesen thinks one reason it has been so tricky to unpick differences between obesity-prone and obesity-resistant individuals is that the majority of studies compare people's metabolisms over 24 hours, which is "just a snapshot". He sees obesity as a failure in the overall system of nutrient sensing, so to fully understand it he believes you have to take a holistic approach, looking at metabolism, appetite and movement over days or weeks.

Using this approach he has found that two days after overeating, obesity-resistant people report an aversion to energy-rich foods such as cake, and their brains become less responsive to images of them compared with obesity-prone individuals. In addition, obesity-prone people become more lethargic two or three days after overeating, whereas their obesity-resistant counterparts remain as active as ever. "I think it's not one thing – it's a whole body response to overfeeding that just works better in a thin person than in an obesity-prone person," he says.

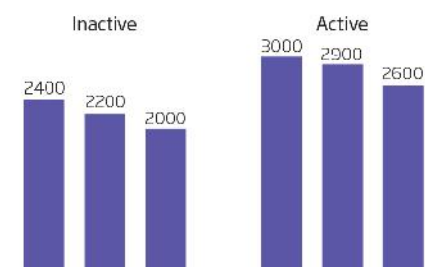
There may yet be other, overlooked mechanisms controlling appetite and metabolism. Studies in mice suggest that transplanting gut microbes from fat animals makes the recipients gain weight, while the gut microbes from thin animals can trigger weight loss. One theory is that the amount of nutrients you extract from food depends on the microbes you possess – although some studies

Middle-aged efficiency

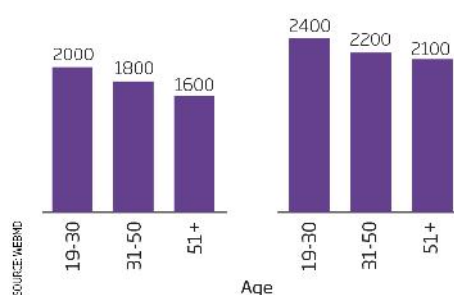
As we age, hormonal changes decrease our metabolic rate so that we need fewer calories

Estimated kilocalorie requirements per day

Male



Female



SOURCE: WEBMD

Age

indicate little difference in the calorie content of faeces between individuals. Another idea is that our microbes are monitoring our food intake and releasing substances that might affect our appetites or the amount of fat we burn. "We have to think of the microbiota as an organ, which is busy sending signals to the rest of the body," says Lee Kaplan at Massachusetts General Hospital in Boston. "It's talking from the position of being the first place that senses nutrients."

There are still plenty of unanswered questions about metabolism, not least whether there is a reliable way to boost it to help people lose weight. One possibility might be to use faecal transplants from thin people – but first we need a better understanding of how microbes shape our metabolism.

Then there's oxyntomodulin, the appetite-suppressing and metabolism-boosting hormone, produced naturally whenever we eat. Pilot studies in obese people suggest that regularly injecting it might aid weight loss. Bloom is about to launch safety tests ahead of a larger clinical trial. "We don't anticipate anything going wrong, but it is still at least 10 years away from being marketable," he says.

What is clear is that metabolism is phenomenally complicated, so anyone who suggests a quick fix to boost it is probably being disingenuous. But don't despair. Provided you can distinguish fact from fiction there are some things you can do that will help (see "14 myths and maybes about burning fat" below). Though it's slightly annoying that people like my husband remain slim with so little effort, I know that if I adopt some new habits, over the weeks and months they should gradually add up. Then maybe, once in a while, I too can overindulge with impunity.

14 myths and maybes about burning fat

There's no end of pop wisdom about why we gain or lose weight, from "fast" metabolisms to what time of day you eat. Here's what science really says.

Skinny people have higher metabolisms – Myth

Generally, the opposite is true: the larger you are, the more calories you need to burn each day just to keep your body going. But there may be some exceptions. Mutations in a gene called KRS2, which reduce the ability of cells to metabolise glucose and fatty acids to provide energy, are twice as common in obese people as slender ones. But they are still rare.

Middle-aged spread is inevitable – Maybe

Ageing triggers hormonal changes in both men and women, and these can influence your predisposition to weight gain. Declining testosterone levels in men reduces muscle mass, which in turn decreases overall metabolic rate, while changes in the balance of female hormones like oestrogen can boost appetite and may dampen metabolism. But weight gain isn't inevitable if you remain active and eat a bit less as you age.

Thin people digest less food – Myth

When Claude Bouchard at the Pennington Biomedical Research Center in Baton Rouge, Louisiana, compared people's stools, he found little difference in their energy content regardless of how predisposed they were to gain weight. Typically, about 3 per cent of the calories consumed are excreted in the faecal matter, he says. "This doesn't change following overfeeding."

Turn down the thermostat to lose weight – Maybe

Babies are born with large deposits of brown fat, which actually burns fatty acids to generate heat. Adults were thought to have none, but we now know that slender adults have some. What's more, volunteers exposed to 15 °C temperatures for 6 hours a day for 10 days while wearing only shorts and t-shirts showed increases in brown fat.

Sleep can make you thinner – Maybe

Sleep deprivation is thought to make you hungrier than usual, as it decreases your levels of leptin, the "fullness hormone"; increases ghrelin, the "hunger hormone"; and impairs normal release of insulin. However, too much sleep also increases the risk of obesity.

Dieting permanently reduces your metabolic rate – Myth

Dieting will depress your metabolic rate. Indeed, the very act of eating increases it, through the release of a hormone called oxyntomodulin, which also blunts appetite. However, there's little evidence for the idea that you inevitably regain all the weight you have lost because repeated yo-yo dieting permanently blunts your metabolism. In fact, crash dieters and those who lose weight more slowly ultimately regain the same amount.

You continue to burn calories after exercising – True

After exercising your metabolism is elevated as your body recovers and repairs itself. This "afterburn" lasts for between 3 and 24 hours depending on the duration and intensity of exertion. The effect tends to last longer following resistance exercises such as weight-training than endurance exercise but, even then, it is pretty small and tails off with time.

Exercise on an empty stomach to burn more fat – Maybe

"If you eat before workouts you will have a little more glucose, which might mean you can work harder," says Michael Ormsbee at Florida State University. "But if you go in fasted, you will probably burn fat faster – although you might not be able to maintain the same level of intensity." He recommends combining both strategies.

Nutritional supplements can boost your metabolism – Maybe

Many are touted. Most probably don't work. There is some evidence that caffeine, creatine, beetroot juice and fish oil have some effect on your athletic performance, says Ormsbee, but it is likely to be tiny, and you would be better off improving your regular diet than taking supplements.

Eating more frequently boosts your metabolism – Myth

While eating temporarily boosts your metabolic rate, it also affects your body's response to insulin – the hormone that regulates levels of glucose in the blood. In a recent study, men were fed the same diet, either as three meals or 14 snacks. Those who ate less frequently had higher metabolic rates, were less hungry and had better control of blood glucose.

Some foods are actively slimming – Maybe

Contrary to popular belief, the caffeine in coffee and green tea won't increase the rate at which you burn fat while exercising, but it may reduce your perception of pain and exertion, allowing you to exercise for longer. Capsaicin – the substance that gives chilli peppers their heat – may increase energy expenditure by boosting the activity of brown fat. A substance in grapefruit seems to improve the body's response to insulin. And a recent study suggests that fibre suppresses appetite.

Eat fat to burn more fat – Myth

A review of 10 studies found little difference in people's overall metabolic rate, regardless of whether they ate a high fat, low carb diet – like the Atkins diet – or a low fat, high carb one. Protein might make a difference, though. People eating a high protein, reduced carbohydrate diet burned between 60 and 120 extra calories a day, possibly because protein requires more energy to digest than refined carbs. Protein is also thought to boost the feeling of fullness.

You have to "feel the burn" to get results – Myth

Running at 6 kilometres per hour burns exactly the same number of calories as walking at 6 km/h. What really matters is endurance. A 73 kilogram person who burns 74 calories per kilometre running at 11 km/h and 52 calories per kilometre walking at half that speed will actually burn 30 calories more walking 2 kilometres than running 1 kilometre.

Eating at night will pile on the pounds – Maybe

"If you want to eat sugar or carbohydrate it's probably better to do it in the morning because your sensitivity to insulin is better then," says Karine Spiegel at the Centre for Neuroscience Research in Lyon, France. "If you eat it during night time you are more likely to store it as fat." This might help explain the finding that a high calorie breakfast and low calorie dinner produced greater weight loss than a small breakfast and large dinner.