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Why your real age may be older – or younger – than your years

Biological age can diverge from the number of years we celebrate on our birthdays - and it sheds light on the time we have left

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By **Helen Thomson**

AGE is a peculiar concept. We tend to think of it as the number of birthdays we have celebrated – our chronological age. But this is just one indicator of the passage of time. We also have a biological age, a measure of how quickly the cells in our body are deteriorating compared with the general population. And these two figures don't always match up.

Just take a look around: we all know people who look young for their age, or folks who seem prematurely wizened. Even in an individual, different parts of the body can age at different speeds. By examining how chronological age lines up with biological age across the population, researchers are starting to pin down how these two measures should sync up – and what it means for how long we have left when they don't.

In recent years, studies have shown that our biological age is often a more reliable indicator of future health than our actual age. It could help us identify or even prevent disease by tracking the pace at which we're getting older. It may even allow us to slow – or reverse – the ageing process.

I became interested in my biological age after discovering in my 20s that my ovaries were ageing prematurely. Yet now, at 33, I am still often asked for identification when buying alcohol, suggesting my face is holding up pretty well. It made me wonder about other aspects of my biological age, and whether knowing more might help me to live a longer, healthier life. So, I set out to answer the question: How old am I really?

Ageing is the progressive loss of function accompanied by decreasing fertility and increasing mortality, according to Thomas Kirkwood from the Institute for Ageing at the University of Newcastle, UK. Surprisingly, it's not universal across species. The *Turritopsis dohrnii*, or "immortal jellyfish", can revert to a larval state and turn back into an adult indefinitely, for instance. We don't have that luxury. According to the UK Office for National Statistics, I can expect to live to 83.

"A new idea suggests ageing is a byproduct of how energy intensive it is for our bodies to repair faults"

The most widely cited theory of ageing is that telomeres, genetic caps on the ends of chromosomes, grow shorter each time a cell divides – like a wick burning on a candle. Once these are used up, the cell withers and dies. But a new idea gaining ground suggests ageing is instead a byproduct of how energy intensive it is for our bodies to continuously repair faults that occur in our DNA as cells divide. "It doesn't make evolutionary sense to maintain that process for ever," says Kirkwood. Indeed, several animal studies have shown that genes that affect lifespan do so by altering cells' repair mechanisms. Little by little, faults build up in cells and tissues and cause us to deteriorate.

This is where biological age comes in – it attempts to identify how far along we are in this process. It's not a simple task, because no one measure of cellular ageing gives a clear picture. As Kirkwood says, "Attempts to measure biological age have been bedeviled by the difficulty of taking into account the many different biological processes at work."

Still, a growing number of researchers have taken up the challenge. Before seeking them out, however, I began to wonder whether I could be in for a nasty surprise. When Daniel Belsky and his team at Duke University in North Carolina studied 18 different markers of cellular ageing – including blood pressure and cardiovascular function – in almost 1000 adults, they found that some were ageing far faster or slower than their birth certificates would suggest. One 38-year-old had a biological age of 28; another's was 61.

So if I have an accelerated biological age, does it mean I'm less likely to make it to 83? Studying humans until they die takes a long time, so the causal relationship is tricky to pin down. But an increasing number of studies suggest this is a fair assumption. Belsky's team found that 38-year-olds with an older biological age fared worse on physical and mental tests, for instance. And when James Timmons and colleagues at King's College London examined expression of 150 genes associated with ageing, they found that biological age was more closely tied to risk of diseases such as Alzheimer's and osteoporosis than chronological age.

Braced for a rocky ride, I started the hunt for my real age by looking in the mirror. In 2015, Jing-Dong Jackie Han and colleagues at the

Can we turn back time?
Tim Flach/Getty

Chinese Academy of Sciences in Shanghai analysed 3D images of more than 300 faces of people between 17 and 77 years old, and created an algorithm to predict age. When they used it on a new group of faces, they found that people born the same year differ by six years in facial age on average, and that these differences increase after 40. (See "Written in your face".)

"Some molecular changes in the body can be reflected on the face," says Han. High levels of low-density cholesterol (the "bad" kind) are associated with puffier cheeks and pouches under the eyes, for instance. Dark circles under the eyes can result from poor kidney function or blood circulation. The message is that if we look older than we should, it could be a sign of underlying disease.

The algorithm was developed using a population of Han Chinese people and so far has only been tested in four caucasians. So, as a white woman, I had my face analysed by a similar algorithm designed by anti-ageing company Youth Laboratories in Russia. The result was a win for me: I apparently have the face of a 25-year-old.

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Next it was time to draw some blood. Using 32 different parameters that reflect disease risk, a team at the company Insilico Medicine developed a deep-learning algorithm to predict age. After training it on more than 60,000 blood samples of known chronological age, they used it to accurately predict age from new samples to within 6.2 years. The team found that people whose blood age was higher than their actual number of years were more likely to have health problems. The algorithm is free to use, so after I had my blood taken by Medichecks in London, I plugged in my details at www.aging.ai. Reassuringly, it shaved off a couple of years, estimating my real age to be 31.

Another method for measuring biological age is to look at how complex carbohydrates called glycans are attached to molecules in the body, a process called glycosylation. Gordan Lauc and colleagues at the University of Zagreb in Croatia recently discovered that glycosylation of an antibody called immunoglobulin G changes as we get older, and that this can be used to predict chronological age. When Lauc's team compared 5117 people's "glycan age" with known markers for health deterioration, such as insulin, glucose, BMI and cholesterol, they found that those who scored poorly on these markers also had an older glycan age.

"Your glycan age seems to reflect how much inflammation is occurring in the body," says Lauc. Prolonged inflammation can make cells deteriorate faster, so having an accelerated glycan age could be used as an early warning signal that your health is at risk, he says.

Lauc and Tim Spector, a genetic epidemiologist at King's College London, founded GlycanAge – a company that tests people's glycan levels – and kindly tested mine for free. It turns out my glycan age is just 20, a whopping 13 years younger than I am.

With a new spring in my step, I moved on to what is now considered the most accurate way to measure human ageing: an intrinsic "epigenetic" clock present in all our cells. Epigenetics refers to the process by which chemical tags called methyl groups are added to or removed from DNA, which in turn influences which genes are switched on or off. Some changes in methylation patterns over time can be used to estimate age.

The father of this technique is Steve Horvath at the University of

California, Los Angeles. In 2011, looking at methylation patterns in blood samples, Horvath and colleagues were able to predict chronological age to within five years. He has since analysed data from more than 13,000 samples and identified methylation patterns to estimate a healthy person's age to within 2.9 years. "The age estimate is so accurate it continues to amaze me," says Horvath. (Unfortunately, for the purposes of my investigation, at $900 a pop, I decided to give this test a miss.)

Horvath is also interested in discrepancies between our chronological age and epigenetic clock, which diverge most drastically in cancer tissue. Trey Ideker, a medical researcher at the University of California, San Diego, and his colleagues discovered that the epigenetic age of kidney, breast, skin and lung cancer tissue can be almost 40 per cent older than the person it came from.

A recent study by Horvath and his team suggests that breast tissue from healthy women aged 21 appears 17 years older than their blood, which tends to correlate closely with their chronological age. This difference decreases as we get older; for women aged 55 years, breast tissue appears around eight years older than blood. By identifying what the normal differences are, researchers hope to flag outliers. "Ultimately, we want to be able to collect data from a particular organ, or from a surrogate tissue and say, 'wow, this woman has breast tissue that is 20 years older than it should be, so she needs to be monitored more closely for breast cancer'," says Horvath.

"It sounds like science fiction… but in theory it's possible to reset the clock"

Beyond monitoring and aiding diagnoses for diseases, can any of these measures give us a better idea of how much life we have left? There is an association between our epigenetic clock and our time to death, but it's not very accurate – yet.

In his analyses, Horvath found an association between accelerated epigenetic ageing – an older epigenetic age compared with your real age – and time to death. Around 5 per cent of the people he studied had an accelerated epigenetic age. Their risk of death in the next decade was about 50 per cent higher than those whose epigenetic age lined up with their actual years.

If our epigenetic clock is ticking down to our death, is there anything we can do to intervene? Horvath has started studying the epigenetic age of induced pluripotent stem cells (iPSC), which are adult cells that can be pushed to revert to an embryonic-like state, from which they are capable of turning into most types of cells in the body.

The epigenetic age of iPSCs is zero. Transforming normal body cells into stem cells would be an "extreme rejuvenation procedure", Horvath says. You wouldn't want to do it to all of your cells, but perhaps it's a strategy that could be modified to intervene with the ageing process. "It sounds like science fiction, but conceptually it's possible," he says. "All epigenetic marks are reversible so in theory it's possible to reset the clock."

Turn back time

Another promising, if speculative, plan might be to freeze blood stem cells when you are young so that you can use them to reconstitute your immune system when you are old.

Short of miraculous anti-ageing treatments, understanding more about biological age can still improve our health. People told their heart age – measured using parameters such as blood pressure and cholesterol – are better able to lower their risk of cardiovascular problems compared with people given standard information about heart health, for instance. (My heart, I learned, is 28 years old.)

There are not yet any placebo-controlled trials to determine whether certain lifestyle interventions can reduce biological age, and so risk of early death. But Horvath did find that the epigenetic clock is accelerated in the livers of obese people, and ticks more slowly for those who regularly consume fish and vegetables, and only drink in moderation.

Unsurprisingly, exercise also seems to help. In a trial of more than 57,000 middle-aged people, those whose fitness levels resembled a younger person's were less likely to die in the following decade or so. Fitness-associated biological age was a stronger predictor of survival than chronological age.

And we may get more conclusive results soon: Spector is about to begin a trial to see if an intensive exercise and diet regime can reduce glycan age. Han is planning a similar trial to see if exercise can influence facial age.

There is still a long way to go before we can pinpoint the exact ways to reverse ageing. But for now, I'm relieved to know that most of my body is younger than my years would suggest and, in the not too distant future, knowing my biological age could hold the key to preventing disease or even postponing death. I'll happily celebrate turning 34 in the knowledge that my age really is just a number.

How old is my brain?

Just like the rest of our body, the brain can sometimes age quicker than we do (see main story). Now researchers at Imperial College London have a way to find out how old the brain really is. James Cole and colleagues trained a computer algorithm to estimate age based on brain images from 2001 healthy people, then tested it on a new group of people to see how old their brains seemed to be.

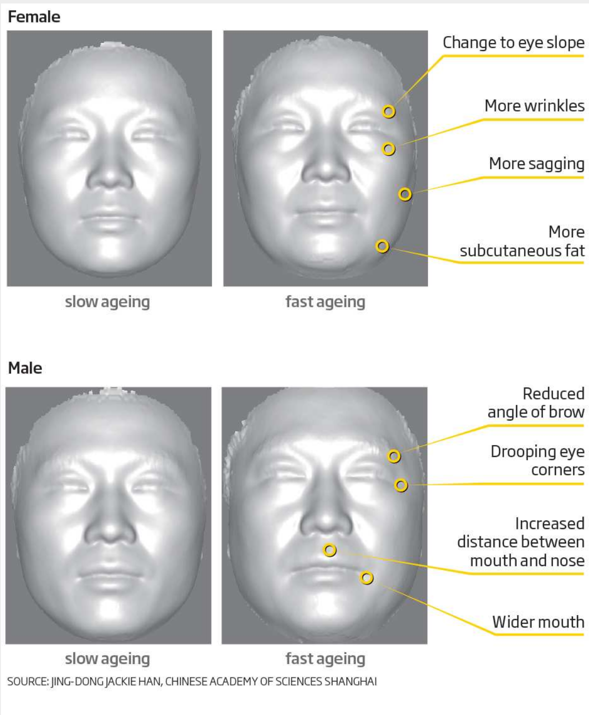
They found that people whose brain age was older than their chronological age had poorer lung function, slower walking speed and an increased risk of death. Those with older brains also performed worse on tests of logic and pattern recognition.

What makes the brain age prematurely? High blood pressure, smoking and high cholesterol seem to accelerate brain ageing, possibly by affecting the blood vessels that carry oxygen and essential nutrients. Long-term stress has also been shown to speed up memory loss in older adults. And shift work has a big impact: more than 10 years of shift work can accelerate brain age by around 6.5 years.

Exercise seems to be key to mitigating these harms. The brains of elderly people who regularly exercise look 10 years younger than those who don't.

Written in your face

After taking 3D images of 300 faces, Jing-Dong Jackie Han and colleagues at the Chinese Academy of Sciences, Shanghai, created composite images of people of the same chronological age (about 45) but markedly different facial ages. Older looking faces are characterised by more wrinkles, wider mouths and several other factors (see diagram). For most of these things, men and women are equally affected. But there are two notable differences. As men get older, their noses protrude more – something that may have to do with the effect of testosterone on cartilage growth. For women, the buildup of a certain kind of cholesterol can make the face appear more "fleshy", particularly in the cheeks and under the eyes.



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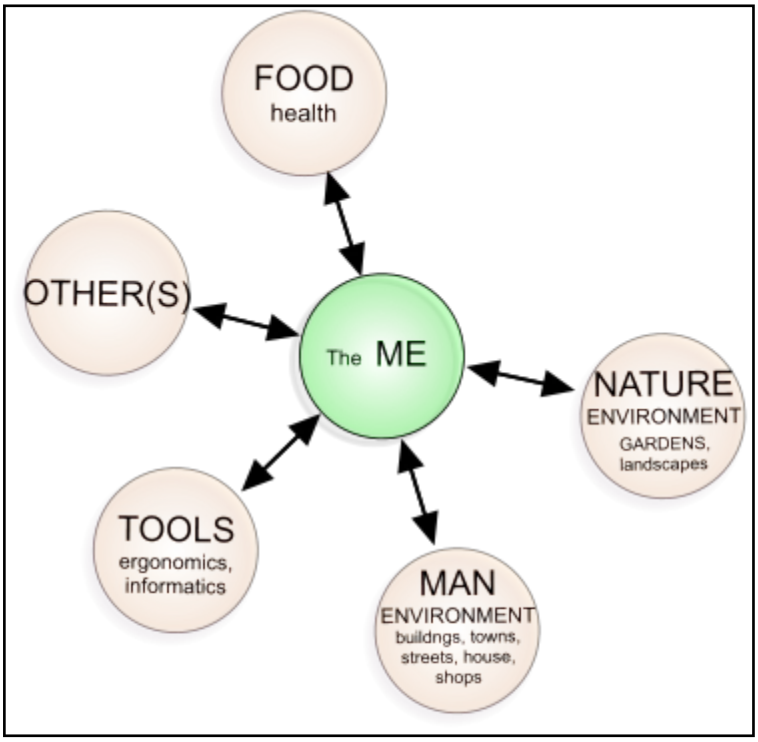
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