

HEALTH

The search for the secret to eternal youth has been going on for centuries and in a way it still continues today. Scientists are still trying to understand exactly what causes us to age — and what causes us to die. As life expectancy rises, the question of how long we can live becomes increasingly relevant. For others, however, the priority is to enter old age with dignity and energy.

Hope springs eternal

Gonzalo Casino examines the mysteries surrounding the ageing process

How long can a human live? The answer to this question varies, depending on dozens of factors, from genes to environmental conditions and the average life expectancy of those around you. The average life expectancy of the world's population doubled during the 20th century. Spain is one of the countries where people live the longest, with men dying at an average age of 76 and women 83. Infections that once killed hundreds of young people are now kept in check with antibiotics, vaccines and other medical advances. The majority of the population make it to old age, and new developments in the field of biomedicine are expected to help lengthen life expectancy even further. But is there a limit to longevity? And if so, where is that limit?

"If we control the three biggest killers in western societies — cancer, cardiovascular diseases and neurodegenerative illnesses — we could reach 100 years of age," says Manel Esteller, a researcher on ageing and cancer at the National Oncological Research Center (CNIO).

But there is still a long way to go until the average life expectancy of a country like Spain can be pushed up to 100. It would mean that while some people would continue to die young, at least half of the population would live for over a century and many others would live to 110 years of age or more. Right now, the reported limit for human life is "122 years of age, which is the age at which the oldest person in the world, Jeanne Clement, of France, died," says Maria Blasco, a researcher on age-

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ing and cancer and deputy head of research at the CNIO.

Until not too long ago the study of ageing was not a respected scientific field, often being linked to superstition and the centuries-long search for a magical formula for immortality. But things are changing. "It's time to start studying the matter in a scientific way. We finally have the genetic knowledge and the molecular tools to do so," says Carlos López Otín, an expert in ageing and cancer and biochemistry and molecular biology professor at Oviedo University.

Although there are those who live an unusually long time in every species, old age is not a common development in nature or an end in itself of the evolutionary process. "Ageing is not a natural thing in the strict sense of the word; what's natural is to die young, as a result of an accident,



You're never too old to make a splash, say these pensioners from Barcelona. / CARLES RIBAS

Not everybody ages the same way, but while genes play a role, making it to old age in good mental and physical health is largely the result of personal choice.

"We can't leave it all up to the genes. The environment and our habits are fundamental in determining whether we will live a longer or shorter life," says researcher Manel Esteller.

A 2001 study published in the *American Journal of Psychiatry* listed the seven personal pre-

requisites that, if met before age 50, allow scientists to predict whether somebody has a solid chance of living to a ripe old age, starting at 70 years of age. These prerequisites are: consuming alcohol in moderation, not smoking, having a stable partner, doing physical exercise,

an infected cut, hunger, cold... Fortunately, ageing has become normal among humans, who live a very sheltered, protected life," says Blasco.

Ageing is not a disease, it is a physiological process that starts at the end of youth. Current scientific theories describe it as the gradual deterioration resulting from growing molecular damage to cells and tissues, which paves the way for disease and death.

Every year that goes by leaves its physical mark — wrinkles, sagging skin, hair loss, among other signs — and its behavioral mark, such as memory loss, greater expe-

Lifestyle choices or gene pool roulette?

rience and less risk-taking. Time also leaves its imprint on DNA. "We're unable to repair effectively genetic and epigenetic [those that occur without mutations] lesions in DNA, and protein production is not as effective, so all of our tissues feel the effects," says Manel Esteller. "We're genetically programmed not to age while we're still able to reproduce," adds Blasco. The up to 25,000 genes in the human body allow humans to develop from one single cell and survive, at least until we reach the age of reproduction, but these genes not programmed to help humans age.

keeping at the right weight, having a high educational level and responding to problems in a positive way. All of these are factors that are mostly under an individual's control.

Many scientists believe that the last prerequisite on the list, keeping a positive mental atti-

tude, is absolutely fundamental. "It's important to remain as young in spirit as possible. That is, to keep on smiling, laughing and not take things too seriously whenever possible. I think that's essential," says Felipe Sierra, a researcher at the US National Institute of Ageing.

"Until now we haven't found any gene whose natural function is to cause or contribute to ageing," says López Otín. "This doesn't contradict the fact that our genome includes genes with protective functions that favor longer life expectancies. But there's a big difference between that and there being an ageing program."

In evolutionary terms "living forever doesn't seem advisable," adds Esteller. "There must be a process that prevents our selfish genes from going to waste. Through reproduction those genes leave our aged body and es-

ablish themselves in a new host: our children." While the genetic limit of human life is considered to be around 120 years, that of lab mice is three years. Humans and mice have a very similar genome, but this huge difference shows that evolution has adjusted our genes to a different life limit, altering their functions in the process, explains Blasco. Of course, there is still a big difference between an individual's genetic potential life span and the actual life expectancy of a person or a population. If the two numbers don't coincide that is because our life span is also

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Preparing for the uncharted territory of old age

Quality not just longevity should be the watchword for those bidding farewell to youth

determined by environmental factors — that is, lifestyle and luck. Certainly, having ancestors who have made it past the 100-year barrier boosts anybody's chances of living a long life. But life itself is like a poker game, we might start off with a better or worse hand in the shape of good or bad genes, but from there on it all depends on luck and on how we play our cards.

Some life-long studies on twins show that genes can determine up to a degree of 40 percent how long we will live. And yet, genes and the environment "are hard to separate, because they are part of the same equation," says López Otín. "People with genetic variants that favor longevity must live in the right environment to allow that molecular advantage to express all of its potential. And the opposite is true too: the right environment can minimize certain negative factors in our genome."

Evolution has neglected the development of organisms beyond their reproductive age. From that point on, the biological mechanisms that protect us from deterioration stop working quite so well and we grow old. Currently, most scientific studies link ageing to cancer. Not surprisingly then, most experts in the field of ageing are also cancer experts. "The more resistant we are to cancer the later we age and vice versa. Humans are very resistant to cancer and age late. Mice, on the contrary, age early and are a lot less resistant to cancer," says María Blasco. "That means that cancer and ageing have evolved together." There are genes whose function conditions cancer to the same extent as ageing. If those genes are altered, the two processes can be altered too.

One of the mechanisms that protect humans against cancer is the shortening of the telomeres, the structures located at the tips of chromosomes. Every time cells multiply to regenerate tissue, the telomeres become shorter and the DNA becomes more vulnerable. "The shortening of the telomeres is one of the proven molecular causes of mortality," says María Blasco. In fact, if the shortening of the telomeres is avoided, cells can become immortal. This can be done through an enzyme known as telomerase, "the enzyme of immortality."

"For the time being, neither medicine nor biology offer a specific, scientific and attainable possibility of intervening in any significant manner in the human ageing process," explains López Otín. But there are a number of specific measures that could partially influence certain aspects of ageing, he adds. For instance, it is possible to reduce the levels of free radicals that result in damage by oxidation of the cells, which would imply awarding them some protection.

Scientists have already managed to lengthen the average life expectancy of mice by 25 percent by limiting their caloric intake, but the genetic mechanisms responsible for these effects of hunger are not yet clear. It is also unclear whether the same would happen to humans, although there are some ongoing experiments — including the use of drugs to reproduce in biochemical terms the effects of caloric restrictions, like resveratrol — that expect to be able to offer answers to this question in a few years time. As for publicized hormone treatments such as those based on the growth

RAMÓN BAYÉS
Every month an average of 36,000 people turn 65 in Spain. Although many, if not most of them, are in good health, they are on the threshold of what is called old age. There is currently a great deal of debate on the issue of population ageing, making it all the more timely to go back to some of the thoughts expressed in a little-known book by one of the most controversial psychologists of the 20th century. B.F. Skinner was 79 when he wrote *Enjoy Old Age*.

In the first pages of the book, Skinner establishes the fact that people in the western world live longer and suffer less than in the past from poverty and disease as a positive development. At the same time, however, he highlights that if during these extra years people don't make the most of their lives then the gains will have been very limited. Technological advances have helped solve significant health problems and given people more years to enjoy their lives, but at the same time they have created a whole new set of problems.

When a person decides to travel abroad he or she tries to find out as much as possible about the chosen destination, about its monuments, museums, history, habits and climate. It is not unusual to even try to learn some phrases of the local language and if possible, to find other people who have already visited that place to get extra, first-hand information. Old age is very similar to a different coun-

"Wouldn't old age at 800 be just as difficult as old age at 80?" asked Cicero

try from the one in which people live most of their lives, and making the most of those years would be easier if people got ready for the trip before embarking on it. But contemporary societies prefer to ignore old age and live as if it were a non-existent place. And then suddenly, when they least expect it, it catches up on them

hormone to combat ageing, their validity has been questioned by a recently published study, says López Otín.

Every 10 years all the cells in the human body are renewed thanks to the regenerative potential of stem cells, but there is a limit to this regeneration. The use of stem cells could in theory shatter that limit and allow us to cure



Alcalá de Henares University teacher, Antonio Molero, keeps his mind in motion. / U. M.

before they have managed to get ready for it: for instance when a young lady gets up to offer them her seat on a bus.

It's an interesting paradox: while everybody wants to make it to old age, nobody wants to be old. "Wouldn't old age at 800 be just as difficult as old age at 80?" asked Cicero. Despite this, it is possible to come up with an appealing brochure for old age. Instead of accepting passively its pains and deterioration, and suffering in silence like many other elderly people, why not confront it as if it were a problem to be solved by increasing the chances of making the most of it?

Retirement brings about all kinds of changes. But if those who are going through it are not among the lucky group of people who can keep on doing the same or similar activities to those they managed to do suc-

cessfully in the past — for instance as a result of early retirement or because they are not able to fend for themselves anymore — they must find other things they would like to do, because otherwise all that awaits them is boredom and depression. Retirement must certainly be considered a social milestone, but when it is forced upon someone irrespective of his or her productivity and love for the job, it is a form of age discrimination.

Not long ago, Antón Costas wrote in EL PAÍS: "Does it make sense for the official retirement age to be kept at such a young age as 60 or 65? Is it right to enforce such a radical and complete break with the working world rather than it happening as a gradual process? My impression is that the users' manual for retirement has yet to be written."

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animal species, such as worms and flies, via gene manipulation. The challenge now is to use the same mechanisms to lengthen a mammal's life. Until now only minor increases in the longevity of mice have been attained through genetic modifications. María Blasco's research team at the CNIO has attained some success by lengthening the telomere which

When Skinner writes about making the most of old age, he highlights the need for old people to identify a series of things they enjoy doing. It is not about the reasons that make people do something, but about what happens to them while they are doing them. Those who can't keep on doing what they were doing beforehand must find new, interesting activities to explore, be it writing, painting, growing a vegetable patch, cooking, going to the gym or getting a university degree.

Before old age hits it is important to undergo some training to be able to put on a good performance during this complicated stage of life. What younger generations tend to expect of elderly people is not particularly flattering. The stereotype of an elderly person is often that of an ill-tempered, tight-fisted, whining, boring, demanding, insensitive and selfish individual. To an extent it is rather easy to be old and act this way, and by acting this way — even occasionally — the stereotype will be reinforced.

Why not transform the stereotype and make the traits that define an elderly person the following: serenity, generosity, dignity, warmth, wisdom, freedom and a sense of humor? "Are these character traits of some elderly people exceptional?" wondered Skinner, "or are they just the features of normal people under exceptional circumstances? If that's the case, would it be possible to alter the circumstances in such a

The elderly need a new activity — be it writing, painting or growing vegetables

way that all those who play the role of the old man can put on a better performance?" Perhaps a good way to start would be to place on our front doors the motto of the San Egidio Community: "Long live the elderly!"

Ramón Bayés is a professor at Barcelona's Autonomous University

has also helped make mice more resistant to cancer. This kind of genetic manipulation, however, is not an option in the short or medium term. "There are more important problems, such as knowing our limits and exploring the molecular world of each cell before embarking on the pursuit of impossible dreams of immortality," says López Otín.