Petite and Old: How Body Size Affects Lifespan

by Désirée Ferrari

My grandmother Onésime died at 115 years of age. Everybody used to call her by her surname *"Topo"*, which means "mouse" in Italian, because she was only 1.52 meters tall and weighed 50 kg when she was pregnant at term. Her two brothers and four sisters were all much taller and stronger than her. Even though they were all born and raised in the same small idyllic village up in the mountains in northern Italy, none of my grandmother's siblings lived long enough to see their 85th birthday.

The family house on the slopes of Mount Rosa. (Photo: Désirée Ferrari)

What determines the lifespan of an individual? Almost a century ago, the German physiologist Max Rubner coupled the maximum life span potential of different species of animals with their size and their metabolic rate, claiming that a guinea pig is smaller than a horse, has a higher metabolic rate and therefore it "burns out" quicker, thus reducing its life span. This widely accepted theory does not explain why birds and mice, although having similar body sizes, have different lifespan. For example, under ideal conditions in captivity, a house mouse can live four years. Meanwhile, a broad-billed hummingbird (which is a quarter the size of the mouse) can live up to fourteen years *in the wild*.

Another observation that questions the correlation between increased lifespan and lower metabolic rate, is the effect of voluntary exercise. We know that regular physical activity

increases the metabolic rate of humans and rats. At the same time, a study published in the journal Circulation found a correlation between exercise and increased life span: *"A substantially lower risk of mortality was observed among individuals who had adequate levels of both long-term leisure time moderate and vigorous physical activity"*, the study says, noting that while the physical activity guidelines recommend that adults engage in at least 150 to 300 minutes per week of moderate exercise, if adults do more than the recommended amount, it can lower their risk of death.

Is there any scientific explanation for the long life of my grandmother, and more importantly, what are the theories behind some experimental treatments that try to extend longevity?

Humans are extremely long-living mammals, both for our size and in absolute terms. We have an expected medium lifespan that is four to five times longer than the one of similar-sized domestic mammals (pigs and sheep can live up to 25–27 years, compared to more than 100 years for homo sapiens). The longevity record for the blue great whale is only 110 years while the oldest person ever whose age has been independently verified is Jeanne Calment (1875–1997) of France, who lived to the age of 122 years and 164 days.

The natural aging process in mammals has four characteristics: it is progressive, irreversible, deleterious for the individual and inherent to the individual, that is, can be affected by external factors but is mostly genetically determined. The village where my grandma Onésime *"Topo"* was born in 1880 lies high on the slopes of the Mount Rosa massif. It was as isolated from the turbulences of European politics and the temptations of industrialization as one can imagine. I can remember my teenage summers there during late 1980s and my frustration with the old black and white TV that only worked if the weather was clear. In this isolated environment, we can assume that my grandmother's siblings (which all surpassed age 75 years – and all of them being high-functioning even during their later years) might have experienced similar external factors, for example with regards to exposure to environmental pollutants. A number of studies correlate the exposure to air pollutants with a shorter life span and with the onset and progression of various diseases through direct effects and by modification of the individual's genes.

In a review article published in 2020, the Italian medical researcher Agostino Di Ciaula comments: *"Almost all environmental factors generating detrimental effects on aging are modifiable, with relevant implications in terms of primary prevention measures potentially leading to decreased frailty, to an increase in the number of years lived without diseases or disability, and to a significant reduction in health expenditure."* Personally, though, I love my life in the city, and even if I force my teenage daughters to mobile-free vacations in Italy (although the thought of a life in idyllic isolation would be considered by them as a violation of the Convention on the Rights of the Child). Therefore, I can only choose to live as environmentally friendly as possible and hope that I have inherited my

grandmother's genetic material for longevity. But if I want to be sure to increase my chances of a long life, I might need to dig deeper and find additional routes to longevity.

Back to Onésime *"Topo"* – she was well known for happily surviving an active working day with an egg and some slices of whole meal bread in her tummy. She laughed and went on bragging that during the war, she could do without the egg – but she was younger then. Calorie-restriction has been shown to increase longevity in different organisms – all the way from yeast to non-human primates. There are more and more published data showing that longer periods of calorie restriction without malnutrition improve risk factors involved in the development of different illnesses, such as diabetes, infarct, cancer, and neurological disorders in humans.

However, being on a low calories diet for a long period of time is not for everybody. Studies in humans show poor adherence, in part because of the ready availability of energy-dense foods and drinks within modern society. Another dietary strategy that has been used with better long-term success is intermittent fasting. Various forms of intermittent fasting have been proposed, which involves restricted energy intake for periods of twelve hours or more per day, or for 24 hours on alternate days, or even eating normally during weekdays and then fasting during the weekend.

These prolonged periods of energy restriction are thought to elevate the metabolism of specific substances such as ketones, fatty acids and glycerol, and stimulate adaptive processes that improve body composition and physiological function. However, the research in this field is still in its infancy and at the moment, the correlation between intermittent fasting strategies and prolonged lifespan is not well established.

Curiously, the research also shows how the temperature of the body tends to decrease in organisms during calorie-restricted diets, while at the same time there are studies demonstrating that reduction in body temperature itself could prolong longevity independently of the amount of calories in the diet: in one of these studies, several mutant mice with a lower body temperature lived constantly more than their warmer companions.

However, with my Italian heritage, I am a huge fan of both warm climate and good food, so I feel a creeping frustration while I dive into this interesting, ground-breaking but not yet problem-solving field. Fortunately, researchers have also looked into the possibility of anti-aging drugs and obtained promising results in laboratory settings. In this regard, it seems that more is better – if the action of a single drug can prolong the life of a fruit fly, a combination of different drugs all aimed at affecting the same cellular processes appears to be the future of the anti-ageing therapy. At the moment, this technique has only been tested in experimental conditions in fruit flies, but I'm prepared to stand in line, waiting for the first humans trials.

During one of our last summers together, I actually asked my grandma the secret to her longevity. She looked at me deep in the eyes, shook her head a moment and answered: “Do not die young.”

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