Man has overcome the power of natural selection. He no longer adjusts to the conditions of external environment, but creates around him an artificial, beneficent environment, remaking nature. He does not need death as a factor accelerating the improvement of humanity from generation to generation. …

There are no theoretical prohibitions to raising the possibility of immortality. I am deeply convinced that, sooner or later, the era of longevity will arrive. … As in any task, enthusiasts are needed for this, unfortunately these are very few; we are hindered by the deep-rooted conviction that death is inevitable and that the struggle with it is futile. This is a sort of psychological barrier that must be overcome.


Theme of the month: Blood and rejuvenation

Some history

For thousands of years, blood has been one of the elements of the body with the strongest symbolic representation, representing in particular life, heredity (blood ties), fidelity (exchange of blood) and mechanisms of rejuvenation.

Considered to be one of the most ancient acts of medicine, bloodletting probably originated in Ancient Egypt, but also in the oldest traditions of India and the Arab world.

In Greece, Erasistratus, in the third century BC, taught that diseases result from an overabundance of blood: the plethora.

In the second century AD, Galen professed that good health requires a perfect balance of the four "humors": blood, phlegm, yellow bile and black bile. His writings and teachings made bleeding a common technique throughout the Roman Empire.

In medieval Europe, bloodletting became the basic treatment for all diseases, in particular, plague, smallpox, epilepsy and gout.
The technique then was to cut veins or arteries in the forearm or neck, using a special tool with a sharp blade.

Bleeding, as a medical procedure, became a little less distressing in the 18th century: doctors used spring-loaded lancets and an instrument called a scarifier, with several blades making parallel cuts.

**Young blood**

What if the elixir of youth flowed through our veins? At least among those of us who have not yet dried up the source: the young. The hypothesis, which seems to come straight out of a vampire movie, is being studied more and more seriously since experiments have shown that blood extracted from an organism in the prime of life can regenerate bodies weakened by the weight of years. So much so that, in order to combat the many diseases associated with old age, the first patient transfusion trials have just begun.

A recent article by Harold Katcher and Steve Horvath, among others, concerns two-year-old rats that received blood plasma from young rats. Their physiological indicators during the test had almost become those of 6-month-old rats. This seems promising but this study is controversial, in particular because it does not test longevity and the rat sample is not sufficient to draw reliable conclusions. Moreover, this study has not yet been validated by the scientific community.

Already 15 years ago, this surprising lead in the quest for eternal or at least prolonged youth was opened up by the experiments carried out by Irina and Michael Conboy and their colleagues at Stanford University. “We wondered why all organs age at more or less the same rate, and we thought that the blood that connects them could be an explanation,” says Michael Conboy.

To test this, his team temporarily connected the vascular networks of young and old mice as if they were Siamese twins; a complex surgical procedure called parabiosis. And they found that the muscles and liver of the older mice regenerated more efficiently, while the opposite occurred in the younger mice.

According to results published by an international team led by Tony Wyss-Coray of Stanford University, young blood could stimulate the production of new neurons in older mice. Meanwhile, an Anglo-American team, co-led by Amy Wagers, observed a regenerative effect in the spinal cord.

But where do these "alchemical" powers of young blood come from? Scientists have been trying for several years to identify the molecules that promote this regeneration. Experiments involving the injection of some of them have already produced promising results, and there is no shortage of avenues of research.

Where, on the other hand, may the molecules with the opposite action come from that gradually replace them in the blood over the years? We can imagine that certain tissues or organs, as they age, 'infect' others by producing more and more harmful molecules, which will travel through the bloodstream, says neurologist Tony Wyss-Coray. It remains to identify which ones.
The researcher shares the hope, with many colleagues, that inhibiting the action of these molecules linked to aging, and reinforcing the action of regenerative molecules present in young blood, could slow down the aging process.

While waiting for this Grail of life extension, the objective is already to prevent or treat the many chronic diseases favored by age (cardiovascular or neurodegenerative pathologies, bone and muscle fragility...), but also to promote organ regeneration after an accident or surgery.

And the first human trials have already begun. As early as 2014, Tony Wyss-Coray founded a start-up, Alkahest, which has since been giving weekly transfusions of a few deciliters of plasma, donated by individuals under 30 years of age, and bought from blood banks when they had a surplus, to 18 Alzheimer's patients.

In 2019, the Wyss-Coray team published in *Nature Medicine* concerning a protein, VCAM1, which increases with age and seems to have a significant impact on the brain. Biological and cognitive measurements indicated that blocking VCAM1 not only prevented old plasma from damaging the brains of young mice, but could even reverse the deficits in older mice.

**Diluted blood plasma**

A new study, led by Irina and Michael Conboy of Berkeley University, has revealed an interesting new direction in efforts to combat the effects of aging. The team's research showed how diluting the blood plasma of older mice can have a strong rejuvenating effect on tissues and organs by reducing the concentration of inflammatory proteins that increase with age.

Half of the mice's plasma was exchanged for a solution composed of salt water and albumin. This significantly improved the health of the older mice. The rejuvenation effects on brain, liver and muscles were the same or greater than in the first experiments in 2005. The procedure had no negative or positive effects on the health of the young mice.

Using proteomic analysis to study blood plasma and its protein content, the team discovered that the process acts as a "molecular reset button". After the exchange, the team observed lower concentrations of pro-inflammatory proteins while beneficial proteins, particularly those that promote vascularization, were able to thrive.

"There are two main interpretations of our original experiments (from 2005)," explains Irina Conboy. The first is that in the mouse joining experiments, the rejuvenation was due to young blood and young proteins or factors that decrease with age, but an equally possible alternative is that, with age, you have an increase in certain proteins in the blood that become harmful, and these have been suppressed or neutralized by the young partners. As our (recent) experience
shows, the second interpretation proves to be correct. Young blood or factors that are not necessary for the rejuvenating effect; dilution of old blood is sufficient.

**Drug candidates**

"Some of these proteins are of particular interest and in the future, we may consider them as additional therapeutic and drug candidates" says Michael Conboy. "But I would caution against being overly optimistic. It's very unlikely that aging can be reversed by changes in a single protein. In our experiment, we found that we could do a relatively simple, FDA-approved procedure that simultaneously altered the levels of many proteins in the right direction."

So this is extremely promising. Unfortunately, only markers of aging were measured. No verification of progress in longevity was done since the mice were sacrificed once the experiment was completed. It may well be that the effects are only temporary or even negative over the long term.

However, a double-blind experiment on humans is said to be already being planned. It is very positive if this happens quickly and with well-informed volunteers. We would then quickly know whether there is as positive an effect on humans as on mice. We would know after a few months whether the positive effect is lasting. If it is, it will be a huge advance in longevity.

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**This month’s good news: More and more international conferences for online longevity**

Following the Covid-19 pandemic, a positive collateral effect is a wider, faster and often free dissemination of events concerning longevity. Thus the Life Extension Advocacy Foundation (LEAF - Lifespan.io) broadcasts numerous conferences, in particular via its YouTube channel.

Note for non-English speakers that it is possible to use automated translation for subtitling. It is still imperfect, but generally already understandable. A useful technological advance for many uses, including sharing information for a longer life.

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**For more information, please visit:**

- heales.org, sens.org, longevityalliance.org and longecity.org.
- Source of the image.