



Breathing and Longevity | March 2022 | Nº156 | The death of death

The longevity revolution (...) that is taking place today and (...) will change human life, probably more than any other revolution we have known in human history. (...) A number of very serious scientists are telling us about this longevity revolution.

They are not crazy American billionaires, nor delusional transhumanists. They are, for example, Jean-Claude Ameisen, who was the president of the ethics committee, who is a very serious guy. (...) I have a whole series of quotes from extraordinarily serious medical professors who say that we are in the process of experiencing this revolution of longevity.

Luc Ferry. December 2021. <u>Meeting of the future</u> (translation).

Theme of the month: Breathing and Longevity

Introduction

In the early history of life, for over a billion years, oxygen was a <u>violent poison</u> for the first organisms. This was in the days of single-celled organisms, when organisms were unlikely to <u>age</u>.

Today, oxygen is necessary for the majority of living species. Lungs appeared in marine species at least 420 million



years ago. In humans, lungs are the <u>almost exclusive</u> source of respiration.

In the course of a lifetime, we inhale about 300 million liters of air. One liter of air weighs just over one gram, so the 12 cubic meters we take in and breathe out each day is approximately 15 kilos of gas.

When inhaled, the air is composed mainly of nitrogen (78%) and oxygen (21%). Carbon dioxide (CO_2) accounts for only 0.04% of the air inhaled. Oxygen is needed for the body's metabolism, and carbon dioxide must be removed.

The <u>exhaled air</u> is depleted of oxygen (17%) and enriched with water vapor and CO_2 (4%). On exhaling, the air is also loaded with invisible <u>aerosols</u>. These contain <u>viruses</u> and <u>bacteria</u>, possibly <u>pathogenic</u>, from the <u>respiratory tract</u> and the oral cavity. These aerosols contribute to the phenomenon of contagion, even in the absence of <u>coughing</u> and <u>sneezing</u>.



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The rate of respiratory aerosol tends to increase with age.

Unfortunately, we also absorb these organisms from our relatives as well as many other substances, such as fine particles from pollution, allergens, etc.

Breathing also allows us to use our sense of smell, the fascinating capacity of olfactory cells that allow our brain to distinguish between millions of odors based on minute quantities of volatile substances. With advancing age, these abilities, like others, imperceptibly but, until today, irreversibly diminish.

What are the main lung diseases? Three main categories

- Acute illnesses :

Infectious diseases of the bronchial tubes (<u>bronchitis</u>) or lung tissue (<u>pneumonia</u>). In both cases, the disease is bacterial or viral in origin. Pneumonia can also be caused by a fungus and bronchitis by irritants such as smoke.

The elderly are very vulnerable to these diseases. Aging favors the entry of infections because defenses are weaker and because there are usually other pathologies or chronic diseases present.

Bronchitis is rarely fatal but can become chronic. Pneumonia, on the other hand, can have serious consequences for an elderly person and lead to death. Nearly one in five centenarians dies from pneumonia, compared to only 6% of 80-85 year olds.

- Chronic lung diseases including :

<u>Asthma</u> can develop at any age. When an older person develops asthma, the symptoms are mostly the same as those affecting younger people. However, it is more risky for an older person because they are more likely to develop other respiratory problems.

<u>COPD</u> (Chronic Obstructive Pulmonary Disease) is a common inflammatory disease of the bronchial tubes. It is often the result of heavy exposure to inhaled toxic substances such as tobacco or pollution. In the elderly, it often develops into a respiratory disability requiring oxygen at home.

- Lung cancer :

Lung cancer is primarily caused by smoking, but also by exposure to substances such as asbestos or fine particle pollution. In Belgium, it is the 3rd most common cancer. Every year, more than 3000 people between 60 and 70 years old get lung cancer. The frequency of these cancers increases with age, but decreases after 70 years. It is one of the most dreaded cancers as only 18% of men and 16% of women survive more



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than 5 years.

Why are respiratory diseases more common in older people?

Because aging involves:

- Decreased muscle strength, especially in the intercostal muscles, back muscles and respiratory muscles.
- Decreased cough strength.
- Decreased airway clearance.
- Decreased tissue elasticity due to degeneration of elastic fibers and changes in collagen.
- Inflamm-age" phenomenon.
- Changes in the immune response.
- ...

Medical advances and research

Antioxidants

We can first note that, especially in the past, <u>antioxidants</u> have been considered as a means to fight aging. The idea is that respiration generates free radicals with deleterious effects and that substances can absorb these radicals. However, this concerns respiration at the level of the cell, not specifically the lungs. Furthermore, to date, no antioxidant has demonstrated a significant and undisputed longevity effect.

Gene therapy for lung disease

As far as respiratory diseases are concerned, many are chronic and often of genetic origin.

The lungs are an accessible organ for gene therapy, but the complexity of the lung structure presents certain physical and chemical barriers to the delivery of <u>viral vectors</u>. In addition to these barriers, symptoms such as a thick mucus layer in the case of cystic fibrosis complicate the process.

<u>A study published</u> in the Journal of Clinical Medicine <u>in 2020</u> summarizes the various advances in gene therapy for respiratory diseases such as <u>cystic fibrosis</u>, <u>alpha-1</u> antitrypsin deficiency (AATD) and <u>primary ciliary</u> <u>dyskinesia</u> (PCD).

In recent decades, there have been great advances in gene therapies for respiratory diseases. However, researchers are still working on new breakthroughs due to ongoing concerns about safety, specificity and efficacy.



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Stem cells

As in most of the rest of the body, stem cells are found in the lungs. The use of stem cells for regeneration is <u>being researched</u>. In particular, the <u>creation of organoids</u> is possible, but there are no real direct applications for older humans.

Transplants

Lung and trachea transplants are still exceptional operations. As for other organs, xenotransplantation (organ from animals) and bioprinting (printing of tissues or organs) are also <u>envisaged</u>, <u>but not yet carried out</u>.

And further on

Here, as elsewhere, the combination of growing knowledge, coupled with broad-based commitment and funding, can lead to incremental progress and breakthroughs. For example, the catastrophic effects of covid on the respiratory system of the elderly have been rapidly reduced. This is one of the reasons for the insufficient but significant decrease in mortality from this disease.

Good news of the month: Effective cellular reprogramming in aged mice

It was already well known that the addition of a mixture of 4 reprogramming molecules under the name "Yamanaka factors" to cells can reset epigenetic marks to their original state. This partial reprogramming over short periods of time counteracts the signs of aging and increases the lifespan of mice with premature aging disease.

In March 2022, in a paper published in *Nature Aging*: "<u>In vivo partial</u> reprogramming alters age-associated molecular changes during physiological aging in mice. "In this paper, it is found that long-term partial reprogramming leads to rejuvenation effects in different mouse tissues. And that the duration of the treatment determines the extent of the beneficial effects.

In a recent study conducted by Prof. <u>Juan Izpisua Belmonte</u> and his teams at the Gene Expression Laboratory of the Salk Institute for Biological Studies, researchers performed various long-term partial reprogramming regimes in healthy animals, including at different onset times, during physiological aging.

A first group of mice received regular doses of Yamanaka factors from 15 months to 22 months of age (human equivalent: +/- 50 to 70 years). A second group was treated from 12 to 22 months (human equivalent: +/-



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35 to 70 years). And finally, a third group was treated for only one month at the age of 25 months (human equivalent: +/- 80 years). Unfortunately, for these experiments as for many others on rats or mice, as the animals are sacrificed at the end of the experiment to be able to analyze their physiological state, the real result in terms of maximum lifespan is not known.

Compared to control animals, there were no alterations in blood cells or neurological changes in mice that received Yamanaka factors.

The researchers claim that the rejuvenating effects are associated with a reversal of the epigenetic clock and metabolic and transcriptomic changes. The scientific team is now planning future research to analyze how specific molecules and genes are modified by long-term treatment with Yamanaka factors.

For more information:

- See: <u>heales.org</u>, <u>sens.org</u>, <u>longevityalliance.org</u> and <u>longecity.</u>org.
- <u>Source of the image</u>