Age is More than a Number: Strategies to Optimize your Physiologic Age

Nicole Zanin Lawrence, MD
“Something’s just not right—our air is clean, our water is pure, we all get plenty of exercise, everything we eat is organic and free-range, and yet nobody lives past thirty.”
“Successful Aging is defined as the ability to maintain low risk of disease or disability, high mental & physical function, and active engagement with life.”

MacArthur Foundation Study
Physiology of Aging

**Processes of aging**
- Inflammation
- Oxidative stress
- Mitochondrial dysfunction
- Cellular senescence
- Stem cell exhaustion
- Epigenetic alterations
- Cellular damage

**Age-related disorders**
- Alzheimer’s Disease
- Diabetes
- Cancer
- Disability
- CVD
- Parkinson’s Disease
- Osteoporosis

**Specific disease prevention**
- Delay upstream effects of aging

**Specific disease treatment**
- Mortality

**What we want to do**

**What we are currently doing**
How We Measure Age

* **Chronological age** - number of years lived
  - Really just a number

* **Physiologic age** – age of the cells of the body
Physiology of Aging

The graph illustrates the decline in various physiological functions with age. The y-axis represents the percentage of performance, while the x-axis represents age in years. The functions include:

- Nerve conducting velocity
- Maximum heart rate
- Kidney blood flow
- Maximum breathing capacity
- Maximum work rate (oxygen uptake)
- Female fertility

As age increases, the performance of these functions decreases, indicating a general decline in physiological capabilities with aging.
Physiology of Aging
Interaction between:

- Genes (inheritance) - About 25-30%
- Lifestyle factors
  - Physical activity
  - Diet
  - Exposure
  - Comprehensive medical care
“It is not the older you get, the sicker you get, but rather the older you get, the healthier you’ve been.”
Thomas Perls, MD, MPH

New England Centenarian Study

Welcome to the largest and most comprehensive study of centenarians and their families in the world!

To Discover the Secrets of A Long Healthy and Happy Life...

- “Survivors”- have age-related disease- 45%
- “Delayers”- have age-related disease, but later- 40%
- “Escapers”- never get age-related disease 15%
DISEASE DELAY AND GENETICS

Long-lived individuals show apparent compression of morbidity, with delayed onset of age-related diseases.

- **Control**
- **Age<100**
- **100–104**
- **105–109**
- **110+**

**Frequency trends of favourable genotypes**

- **FOXO3A**
- **CETP**
- **APOC3**

HeLa cells showing FOXO3A protein (red)

*The New England Centenarian Study*
What can you do?

* Maintain or improve modifiable causes of age-related change
  * Exposures- UV radiation, smoking, toxins
  * Psychological well-being- social isolation
  * Exercise
  * Nutrition
  * Medication targeted at disease
  * Follow-up with a good physician for preventive health
* Longevity medications and nutraceuticals???
Preventable Deaths

![Infographic showing potentially preventable deaths from the five leading causes of death: 34% diseases of the heart, 21% cancer, 39% unintentional injuries, 33% cerebrovascular diseases (stroke), and 39% chronic lower respiratory diseases.](https://www.cdc.gov/mmwr)
Exercise

Ponce de Leon
Aging: A state of chronic exercise deficiency?
Only 29% of elderly report any regular exercise.
Exercise for Aging Bodies

Mayo Clinic discovers high-intensity aerobic training can reverse aging processes in adults

March 10, 2017

- Cycling three days a week, with four four-minute intervals of high-intensity cycling, followed by three-minute easy cycling intervals
- Two days a week, they walked briskly on a treadmill for 45 minutes
- Also recommend resistance muscle training two days per week
Caloric Restriction

**Canto, 25**

Although a senior citizen — the average rhesus monkey lifespan in captivity is 27 — Canto, above, is aging fairly well. Outwardly, he has a nice coat, elastic skin, a smooth gait, upright posture and an energetic demeanor. His bloodwork shows he is as healthy as he looks.

**Human equivalent** Meals prepared by Mike Linkevay, 36

- **Breakfast**: fermented soybeans and garlic
- **Lunch**: tofu, konyaku and carrots
- **Dinner**: vegan sausage, kale, tomato sauce and salad

**MONKEY MENU**

- Daily calories: 485
- Monkeys also receive an apple each day.

**NORMAL DIET**

**Owen, 26**

He gets more food, but Owen, above, isn’t aging as well. His posture has been affected by arthritis. His skin is wrinkled and his hair is falling out. Owen is frail and moves slowly. His bloodwork shows unhealthy levels of glucose and triglycerides.

**HUMAN MENU**

- Daily calories: 2,000
- Beverages, snacks and desserts not shown. Diet varies according to body type, sex and activity level.

Diet of an average, active human male of 36.

What is intermittent fasting?

- Cycling periods of fasting 1-3 days per week with non-fasting
- When non-fasting day - one can eat “freely”
- Fast days can be characterized by:
  - water only
  - water and noncaloric beverages
  - very low calorie – such as 500 calories/d (75-90% restricted)
- “Time restricted feeding”
  - Eating only allowed within set hours of the day
  - Example: eat only during 4, 6, or 8 continuous hours per day every day of the week
Energy restriction
  Intermittent fasting
    ↓
    Signal transduction
      Growth factors (IGFs, BDNF, GDNF)
      Neurotransmitters (glutamate, serotonin)
      Calcium influx
        ↓
        Gene expression
          Stress resistance proteins (HSP-70, GRP-78)
          Antioxidants (SODs, GSH)
          Energy metabolism enzymes (ETC and glycolysis)
            ↓
            Enhanced function
              Disease resistance
                Insulin sensitivity
                Decreased blood pressure
                Improved lipid metabolism
                Decreased oxidative damage
A Periodic Diet that Mimics Fasting Promotes Multi-System Regeneration, Enhanced Cognitive Performance, and Healthspan

Sebastian Brandhorst, In Young Choi, Min Wei, Chia Wei Cheng, Sargis Sedrakyan, Gerardo Navarrete, Louis Dubeau, Li Peng Yap, Ryan Park, Manlio Vinciguerra, Stefano Di Biase, Hamed Mirzaei, Mario G. Mirisola, Patra Childress, Lingyun Ji, Susan Groshen, Fabio Penna, Patrizio Odetti, Laura Perin, Peter S. Conti, Yuji Ikeno, Brian K. Kennedy, Pinchas Cohen, Todd E. Morgan, Tanya B. Dorff, Valter D. Longo

15 Co-first author
Published Online: June 18, 2015
Open Archive DOI: http://dx.doi.org/10.1016/j.cmet.2015.05.012 | CrossMark

Article Info
Altmetric 1,441
Promote overall health and longevity and reduce excess fat with our clinically proven 5 Day Meal Program.

ProLon Fasting Mimicking Diet (FMD™) is scientifically proven to positively impact biological aging and related health risk factors.
Resveratrol imitates the genetic effects of caloric restriction.
<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Reduces inflammation</td>
</tr>
<tr>
<td>Bile Acids</td>
<td>Triggers longevity gene pathways</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Blocks mTOR - Enhances insulin sensitivity</td>
</tr>
<tr>
<td>Estradiol</td>
<td>Rejuvenates skin and improves brain function</td>
</tr>
<tr>
<td>Everolimus</td>
<td>Reinvigorates the immune system</td>
</tr>
<tr>
<td>GH3/Gerivitol</td>
<td>Lowers cortisol levels</td>
</tr>
<tr>
<td>Melatonin</td>
<td>Powerful antioxidant</td>
</tr>
<tr>
<td>Metformin</td>
<td>Enhances insulin sensitivity</td>
</tr>
<tr>
<td>Protandim</td>
<td>Activates Nrf2 – a longevity regulating protein</td>
</tr>
<tr>
<td>Rapamycin</td>
<td>Delays onset of degenerative diseases</td>
</tr>
<tr>
<td>Resveratrol</td>
<td>Powerful antioxidant</td>
</tr>
<tr>
<td>Statins</td>
<td>Lengthens telomeres</td>
</tr>
<tr>
<td>TA-65</td>
<td>Lengthens telomeres</td>
</tr>
<tr>
<td>Thymus Extract</td>
<td>Restores immune function</td>
</tr>
</tbody>
</table>
Stayin' alive

Major actions of metformin and calorie restriction

**CELL MEMBRANE**

- **METFORMIN**
  - Insulin
  - Insulin-like growth factor 1

- **CALORIE RESTRICTION**
  - Hormone receptor

- **RESVERATROL**
  - Sirtuins

- **RAPAMYCIN**
  - mTOR

**POSITIVE IMPACTS**
- Inflammation
- Cell survival
- Stress defence
- Autophagy (recycling cell machinery)
- Protein synthesis

**HUMAN LONGEVITY**

Sources: *Cell Metabolism; Applied and Translational Genomics*
Thank you!

Talk to your doctor before doing anything!