

The Urologist's guide to longevity

A primer for the doctor and the patient

Jesse N. Mills, MD

HS Clinical Professor of Urology

Chief, Andrology

Director, The Men's Clinic at UCLA

David Geffen School of Medicine at UCLA

What is aging (senescence)?

- Breakdown of cell processing, faster destruction than construction of new cells.
- Leydig cells begin decline in testosterone synthesis in late 20s and decline 10% decade over decade.
- Loss of Nitric Oxide signaling—this starts around 25 years old!
 - Diminished cardiovascular output
 - Diminished blood flow and smooth muscle activation of critical structures
 - Loss of erectile function

What can you and your patient do?

- You're in my office for an hour a year, the rest of the 364 days, 23 hours is up to you!



What can I, your doctor, do?

- I'm your coach.
- I'm your prescriber.
- I'm your surgeon (but only if you need me!).
My goal is to keep you out of the OR.

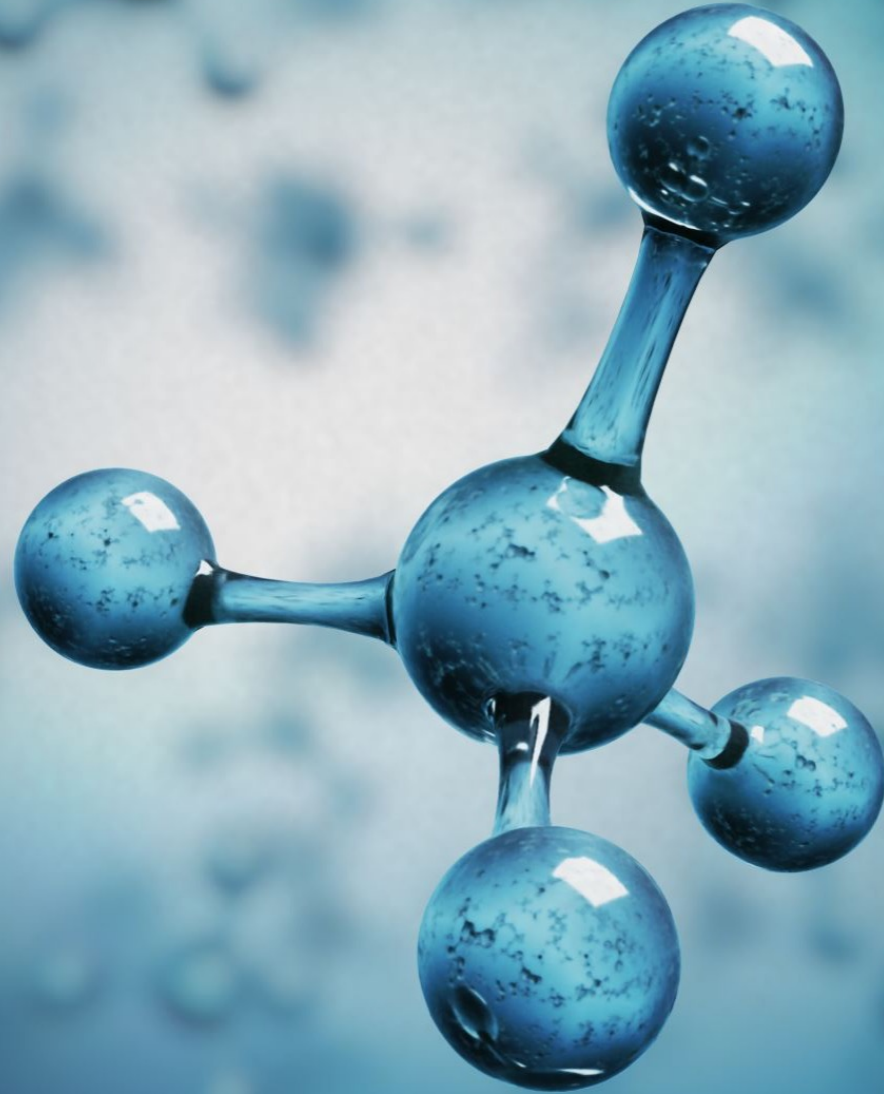


You

- Eat—for most humans, reduce portions, limit meat to 10% of caloric consumption. Avoid processed foods.
- Move—get a heart rate monitor, exercise at 80% of your max for at least 18 minutes 5 days a week.
- Sleep—6-8 hours. Easier said than done.
- Sex—more sex=longer life.
- Have purpose—never retire without a plan
- Add-ons—better health through hottest trends, meh!

The molecules behind the movement

- M-tor
- TNF-Alpha
- Nitric Oxide
- COX-2
- NAD



What about infra-red sauna? Cold plunge?

- Sauna activates heat-shock proteins which are nature's anti-inflammatory. Traditional sauna limited by exposure time before it gets dangerous—infra-red may allow for longer, safer exposure and greater uptake of HSP.

What about infra-red sauna?

Cold plunge?

- Cold plunge? Scientific data are somewhat sketchy. If it feels good, do it (just not right after workouts).
 - Chronic cold-water exposure increases brown fat deposition—brown fat is good for your heart, regulates caloric intake, and improves insulin sensitivity.
 - Maybe increases mitochondrial activity—the energy factory of the cell.
 - Post vigorous workout it can decrease inflammatory mediators which promote muscle repair





Hyperbaric Oxygen

- Stimulates angiogenesis in coronary endothelium, penile endothelium.
- Promotes rapid wound healing by increasing oxygenation of tissues and stimulating multiple mitochondrial enzyme upregulation.
- Decreases apoptosis in high turnover cells in part via m-TOR pathway

Lindenmann et al (2022).

Low Intensity Shockwave Therapy

- Not just for erections anymore!
- Improves joint activity
- Chronic pelvic pain syndromes
- Vertebral angiogenesis, may reduce chronic back pain, improve degenerative disc/s

Shiao-Jin Guu et al. (2020)

Preventative Pharmacology

- We take supplements to not get scurvy, Ricketts, pass on neural tube defects, anemia, and a host of other ailments.
- We don't wait to get these diseases and then start the treatment.



Longevity is Proactive v Reactive medicine

- Predict the problems
 - For the last 10+ years, Obesity, for example, causes more deaths than cigarette smoking—how many 90-year-olds can you think of who are obese?
 - Prepare for prevention. Stay tuned for personalized medicine.
- Don't wait for the pain of disease
 - If you have a history of cardiac disease, take steps, both lifestyle, and pharmacologic, to prevent progression of your genetic dice roll.
 - If you are starting to gain weight, don't wait until you become obese.

What general medications improve longevity?

- Sirolimus—bacterially-derived transplant drug that inhibits cell aging and turnover. Few side effects, namely can suppress the immune system but a very potent natural anti-inflammatory!
- Semaglutides—anyone struggling with obesity, pre-diabetes, and certainly diabetes may benefit from this drug. Diabetes accounts for 25% of healthcare expenditures.
- Metformin—another bacterially-derived drug originally prescribed to tackle type II diabetes but has a role in delaying cancer progression, improving erections and managing weight by improving endothelial cell function.
- Methylene blue—improves velocity of electron transport chain in mitochondria, thereby decreasing oxidative stress, promoting fibroblast proliferation at sites of inflammation (Xue, H. [Cells](#). 2021 Dec; 10(12): 3379.)

Sirolimus

- mTOR inhibitor (mammalian target of rapamycin)
- Robust presence in transplant and oncology literature with excellent side effect profile
- Robust murine data on life extension

Lamming et al (2016).

Metformin

- Hypoglycemic agent that improves endothelial function.
- Improves erectile function at doses of 250-1000 bid.
- Tumor suppressing? Studies in metastatic disease point to slowing tumor advancement by inducing hypoglycemic state.



Methylene Blue

- Not just for vasoepididymostomy!
- Research in:
 - Neurodegeneration/memory loss
 - Skin aging
 - Progeria

Semaglutides

- Natural hormone GLP-1 designed for longer half life to induce longer periods of satiety.
- Can induce weight loss, improve endothelial cell function by reducing Hemoglobin A1C.
- FDA approved at low doses for glucose control, higher doses for medical weight loss, widely used off label for cosmetic weight loss. But is it cosmetic?
 - Excellent data on cardiovascular risk reduction, SELECT trial.

What men's health drugs prevent disease (and can women benefit?)

- Tadalafil
 - One of the first signs of aging is depletion of nitric oxide stores—starts around age 25!
 - Tadalafil will keep nitrous oxide (NO) levels high and may stave off cardiovascular disease, vascular dementia, urinary struggles and, yes, erectile dysfunction.
 - Well-tolerated side effect profile.
- Finasteride
 - In addition to prostate cancer prevention (somewhat controversial), prevents hair loss and benign prostate growth.
- Testosterone
 - Has become the pillar of longevity—idea is to preserve high normal testosterone levels as we age to maintain muscle mass, bone density, libido, erectile function.

Caveat Emptor: Drugs have side effects!

- Sirolimus can make some people more prone to infection, can increase LDL cholesterol levels.
- Semaglutides can cause gastroparesis
- Metformin can cause bad GI upset, lactic acidosis.
- Tadalafil: hearing loss, bad reflux, severe muscle ache.
- Finasteride: loss of libido, nipple swelling, maybe increase risk of aggressive prostate cancer.
- Testosterone: increase red blood cell count to dangerous levels, hair loss, acne.

Can longevity be equitable?

- Yes, to an extent!
- All longevity drugs except the newer semaglutides are generic.
- Intellectual property is the biggest expense.
- Good nutrition is cheap.



What is the investment?

- Lifestyle modification is difficult but can be cheap! Improving daily cardiovascular output can be a brisk walk for 30 plus minutes.
- How much fun is longevity for you? Is living longer worth the extra time or the lifestyle sacrifice? Do you have a partner? All in longevity is tough to do as a solo act.
- If you spend 2 hours extra daily on meal prep, exercise, sauna, cold plunging, testicular tanning starting at age 40 and you live to 100, that's 43,800 hours of longevity quest (excluding leap years) or 5 years of time. Most longevity quests boast adding 8-10 years onto your life. Not a bad ROI if you enjoy those 2 hours.

The Philosophy of Terminally Ill Warren Zevon

(ending on what shouldn't be a down note)

- Enjoy every sandwich.
- My ride's here:

*Man, I'd like to stay
But I'm bound for glory
I'm on my way*

THANK YOU!

Jesse N. Mills, MD
HS Clinical Professor of Urology
Chief, Andrology
Director, The Men's Clinic at UCLA
David Geffen School of Medicine at UCLA