# Secrets to Living to 100 and Beyond

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Cambridge Scholars Publishing

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This book first published 2025

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library



ISBN: 978-1-0364-5333-6
ISBN (Ebook): 978-1-0364-5334-3

To my wife, Johi, and our children, Ookun and Oojung

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# PREFACE

# WHY SHOULD YOU READ THIS BOOK?

A century ago, it was rare if not unimaginable for a person to live to be a hundred years old. Today, it is becoming more and more common for people to reach the century mark. In the late 1800s, the average life expectancy in the U.S. was 40 years. As of 2023, it has nearly doubled to 79 years. That means we are adding two to three years to our expected lifespan each decade, or five to seven hours every day. According to the American Psychological Association's Office on Aging, one out of every four 65-year-olds today will live past 90, and one out of 10 will live past age 95. By 2050, it's expected that ten percent of Americans will be over the age of 90.

But living longer is just half the equation. Being able to age gracefully and live a productive and healthy life in our later years is just as important as extending one's life expectancy. This is where the real challenge lies.

Aging is the greatest risk factor for most human diseases. Clinical signs of aging become apparent in women after the age of 40 with the onset of menopause. Men after age 45 exhibit hair loss, changes in hair color and wrinkles. Age-related disorders adversely affect cells, tissues and organ systems. Short-term memory often declines with age, while hypertension, stroke, type 2 diabetes, chronic kidney diseases, neurodegenerative disorders and cancer all increase in probability.

The good news is that we are accumulating important new knowledge about the science of aging. Every week seems to bring new stories and media reports providing advice on health and longevity. A March 25, 2024 article in *The New York Times* cited a study that suggested following an Italian diet could help you live longer. The next month, an Apr. 27 story in *The Wall Street Journal* profiled Harvard Medical School "star scientist" David Sinclair, who said aging is a disease and has to be treated as such, suggesting that it can actually be reversed. However, many aging experts rebuke such dramatic claims. Unfortunately, it's not easy to sort through all this information, even if you have a scientific background.

Numerous books have been published purporting to offer practical guidance and tips on living longer and healthier lives. Some are based on complex biological theories, while others offer recommendations stemming from anecdotal evidence and testimonials. In 2019, Sinclair pub-

lished *Lifespan: Why We Age and Why We Don't Have To*, in which he cited several testimonials suggesting that taking health supplements could reverse biological clocks. The following year, geneticist Nir Barzilai's book *Age Later: Health Span, Life Span, and the New Science of Longevity* detailed a plan to launch a randomized clinical trial to test whether the anti-diabetic drug metformin has the ability to delay the onset of a group of age-related chronic diseases and whether it also decreases mortality.

This book is an attempt to cut through the clutter. I hope to offer readers a clear and detailed overview of the state of aging research today, so that they can be armed with the most up-to-date strategy on how to live longer and, just as importantly, live healthier. Chapter V presents a practical guide that summarizes the pros and cons of specific strategies and discusses facts, myths and common misconceptions about aging, such as, "Is depression in older people normal?" and "Do people need less sleep as they get older?"

I've been a practicing radiation oncologist for over 50 years, and I've treated hundreds of patients during that time. I've witnessed every aspect of a patient's battle with disease. I've celebrated with people as they conquered their illnesses and headed home to their loved ones, and I've also held their hands in their final hours. I've published over 300 peer-reviewed papers on topics ranging from how ionizing radiation preferentially kills malignant cells to clinical trials involving emerging therapies such as hyperthermia and radiosensitizers. After serving as a tenured professor of radiology and board-certified radiation oncologist at New York's Memorial Sloan Kettering Cancer Center for 25 years, I became chairman of the department of radiation oncology at Detroit's Henry Ford Hospital in 1989. As a physician scientist, I was instrumental in translating emerging fields such as radiosurgery and suicide gene therapy for cancer from the laboratory to the clinic.

My co-contributor, Stephen Brown, Ph.D., is the director of the radiation biology research laboratory and co-leader of the translational oncology program at the Henry Ford Cancer Institute in Detroit. After completing his graduate studies in medical physics at the University of Toronto, he moved to Henry Ford to complete postdoctoral work in my radiobiology laboratory. Since 2009, he has also been a professor of radiation oncology at Wayne State University Medical School in Detroit. In 2022, he joined Michigan State University as a professor of radiology in the School of Human Medicine.

My research team at Henry Ford is among the half-dozen U.S. research institutes comprising the Centers for Medical Countermeasures Against Radiation Consortium (CMCRC), which was first established by the Na-

tional Institutes of Health (NIH) in 2005 as a national security priority in the wake of 9/11. Our aim was to find the mechanisms behind why normal tissues and organs develop long-term injuries after exposure to ionizing radiation, as well as strategies to mitigate damaged tissues and organs. These studies and the knowledge gained are pertinent to the field of aging because the damage from radiation exposure mimics the effects of accelerated aging.

For instance, our research has shown that ionizing radiation causes late (delayed) chronic injury to normal tissues, including chronic inflammation and cellular senescence (deterioration). We successfully reduced such effects by optimizing the use of anti-inflammatory agents (such as ACE inhibitors) and through a combined course of antioxidants and micronutrients. Having established senescence as a source of inflammation, we attempted to therapeutically mitigate radiation-induced cellular senescence. We then extended the scope of our research from radiation-induced cellular senescence to aging in general. In researching radiation-related injuries, we gained insights into the aging process.

Based on our careers spent caring for patients in the field and researching in the lab, I believe we are uniquely positioned to dispel common misconceptions about aging and to provide practical perspectives on the best practices for longevity.

# ACKNOWLEDGEMENTS

The authors are grateful for the expert editorial comments by Dr. Kenneth A. Jenrow. They also wish to thank Dr. Stephen Bondy for his supportive comments that became a short description of the book used for promotional purposes. The authors acknowledge the generous support of the National Institutes of Health and its National Cancer Institute and National Institute of Allergy and Infectious Diseases.

# ABBREVIATIONS

ACE: angiotensin-converting enzyme
AFAR: American Federation for Aging Research
AI: artificial intelligence
AMD: age-related macular degeneration
AMPK: AMP-activated protein kinase
BMD: bone mineral density
CALERIE: Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy
CARG: Cancer and Aging Research Group
CD38: cluster of differentiation 38
CDC: U.S. Centers for Disease Control and Prevention
CiRA: Center for iPS Cell Research and Application
CMCRC: Centers for Medical Countermeasures Against Radiation Consortium
CML: chronic myelogenous leukemia
CR: calorie restriction
CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats
CSF: cerebrospinal fluid *or* colony-stimulating factor
EPO: Erythropoietin
ES cells: Embryonic stem cells
FDA: Food and Drug Administration
FKBP12: FK506-binding protein 12
FMD: fasting-mimicking diet
G-CSF: granulocyte colony-stimulating factor
GLP-1: glucagon-like peptide-1
Hsp90: heat shock protein 90
IRB: Institutional Review Board
IL-6: interleukin 6
IND: Investigational New Drug
iPS cells: induced pluripotent stem cells
MSC: mesenchymal stem cell
mTOR: mammalian target of rapamycin
mTORC1, mTORC2: mTOR complex 1, mTOR complex 2
NAC: N-acetylcysteine
NAD: nicotinamide adenine dinucleotide
NIA: National Institute on Aging

| | |
|---|---|
| NIH: | National Institutes of Health |
| NMN: | nicotinamide mononucleotide |
| NR: | nicotinamide riboside |
| OSKM: | Oct3/4, Sox2, Klf4 and c-Myc, the four transcription factors that can reprogram somatic cells into iPS cells |
| OTC: | over the counter |
| p16, p21: | proteins with molecular weights of 16 and 21 kDaltons, respectively |
| PARP: | poly (ADP-ribose) polymerase |
| PBM: | photobiomodulation |
| PI3K: | phosphatidylinositol 3-kinase |
| REM: | rapid eye movement |
| RNS: | reactive nitrogen species |
| ROS: | reactive oxygen species |
| SASP: | senescence-associated secretory phenotype |
| SCFA: | short-chain fatty acids |
| SCT: | stem cell therapy |
| TCM: | traditional Chinese medicine |
| TGF- β: | transforming growth factor beta |
| TKI: | tyrosine kinase inhibitor |
| TNF- α: | tumor necrosis factor-alpha |
| UV: | ultraviolet |
| WHO: | World Health Organization |

# CHAPTER I

# COMMON MISCONCEPTIONS ABOUT AGING

Western cultures have traditionally been labeled as ageist societies that undervalue their older adult populations. Older individuals are frequently stereotyped as dependent, frail, out of touch, or as a societal burden, with jokes about their inability to use technology or right themselves after a fall. During the 2024 U.S. presidential election, Joe Biden was characterized by both the media and the public as too old to govern, despite his record of accomplishment. On the other hand, Eastern cultures have generally recognized the value of wisdom that comes with age and are often more accepting of older adults, a view based on traditional teachings that senior citizens are wise, experienced and worthy of respect.

We all have ingrained cultural assumptions around what aging will mean. And it's hard to separate fact from fiction when it comes to aging due to the firehose of dubiously sourced information in a social media era of ever-proliferating rumors. Addressing and correcting misconceptions for the general population is a challenge for researchers, physicians and other healthcare professionals. As such, it is helpful to start by identifying some of the most common assumptions about aging. The following are compiled from lists published by the NIH's National Institute on Aging (NIA), Rush University System for Health, Brigham and Women's Hospital and *The New York Times*:

## Depression is normal in older adults

**Facts**: According to the 2022 National Health Interview Survey administered by the U.S. Centers for Disease Control and Prevention (CDC), most older adults are not clinically depressed. Only a small proportion (18.6%) of people aged 65 and over reported experiencing depression, lower than the 21.4% average among all adults. Major depression occurs in an estimated 1% to 5% of older adults living in the general community, and in 13.5% of those who require home health care.

## People need less sleep as they get older

**Facts**: Adults of all ages need the same amount of sleep—generally, seven to nine hours per night—although older adults tend to have short, lighter sessions (i.e. catnaps). The quality of sleep declines with age, as does the time spent in both deep (slow-wave) and rapid eye movement (REM) sleep. Deep sleep plays an important role in growth, memory and immune function, while the REM phase is crucial for cognitive functions such as memory organization. Though sleep patterns change with age, adequate quality sleep is important for everyone's overall physical and mental health. (See details in Chapter V, Section 3, "Sleep as Waste Management.")

## If you live long enough, you're going to develop dementia

**Facts**: Approximately one in nine people (11%) in the U.S. develops dementia after the age of 65, although after 80 this number increases to 50%. The situation is further complicated because signs of cognitive impairment in patients diagnosed with dementia may in fact have been induced as side effects of medications they were prescribed (examples include common drugs such as amitriptyline, aripiprazole, benztropine and carbamazepine, which are used to treat symptoms of depression, schizophrenia, Parkinson's disease and epilepsy, respectively).

Dementia is not a specific disease but rather a general term for brain dysfunction such as memory loss, and a diminishment in social skills and thinking abilities. During normal aging, older individuals may develop mild cognitive impairment, occasionally forgetting names and recent events. Such individuals are not considered to suffer from dementia and may or may not develop the condition. Alzheimer's disease is the most common type of dementia, but early detection and intervention may slow the progression of the disease and help keep people independent. Changes in lifestyle, new medications and neurostimulation have all been shown to slow the progression of the disease.

## If a family member has Alzheimer's disease, I will develop it too

**Facts**: About 60% to 80% of dementia patients have Alzheimer's. But only 5% to 10% of Alzheimer's dementia can be attributed to a family history of the disease. Such individuals carry at least one of three known

Alzheimer's gene mutations, and those with a family history of the disease develop symptoms at an earlier age (between 35 and 45 years).

## Older adults should avoid exercise and physical activity so they don't get injured

**Facts**: One common misconception is the belief that exercise may do more harm than good for older adults, particularly for those with chronic health conditions. However, the facts suggest that exercise and physical activity are good for all ages. Biological and clinical studies have consistently demonstrated that physical activity reduces age-related disorders. Daily walking, stretching and resistance exercise have all been shown to have health benefits. Falls are the most common cause of injury-related morbidity and mortality among older adults. Fall prevention programs that combine exercises focusing on strength, balance and flexibility have been associated with reduced falls in multiple good-quality trials, according to a 2024 U.S. Preventive Services Task Force recommendation statement. (More details regarding exercise and biology are described in Chapter V.)

## Now that I'm older, I will have to give up driving

**Facts**: In 2022, 87% of people aged 70 and older had a driver's license, up from 73% in 1997. However, older drivers are also more likely to be injured in a car accident. In California, if you are 70 years old or older at the time your driver's license expires, you are required to renew it in person. Knowledge and vision tests are required. People with dementia often do not know they are having driving problems, so family and friends need to monitor their driving ability and take action as soon as they observe potential problems. Warning signs of an unsafe driver include getting lost in familiar places; dents and scrapes on the car, fences, mailbox or garage doors; and frequent close calls or collisions.

## Osteoporosis is only a problem for women

**Facts**: Certain demographics are more likely to develop the disease, but people of all races and ethnic groups can develop osteoporosis. Osteoporosis affects about one in five women over age 50, but only one in 20 men. Among women, those of white and Asian descent are more likely to develop the disease.

## If my blood pressure goes down, I can stop taking my medication

**Facts**: Always consult your physician regarding decisions impacting your medication intake, especially if isolated readings of blood pressure show values below the recommended readings. People aged 65 and older should aim for a blood pressure reading of less than 130/80. If readings consistently show high blood pressure, your doctor will prescribe medications. Adjustment to new medications will take a few days to weeks. Sometimes over-the-counter drugs, as well as vitamins and supplements, may affect blood pressure, as can lifestyle changes.

## Anti-aging skin products can "take the years off"

**Facts**: Can face creams and expensive topical treatments really reverse the effects of aging (wrinkles, sagging skin, age spots, etc.)? The short answer is yes, but the effects are temporary. Exfoliating the top layers of skin or injecting botox into wrinkles have temporary effects but do not reverse the aging of skin.

## Old dogs can't learn new tricks

**Facts**: Old dogs can learn new tricks (like navigating the internet) if they want to, even though it may take more time. Research demonstrates that neuronal growth, or neurogenesis, does take place in the hippocampus of older individuals who are active, albeit at a slower rate than in younger people, which implies that they can indeed learn and retain short-term memories.

## Older folks are lonely

**Facts**: Although more older people live alone in the U.S. than in other countries, there are ways to combat loneliness. Staying active by helping to care for family members, volunteering or starting a hobby are all ways to feel productive and remain connected with others. Studies show that people who participate in meaningful activities which bring a sense of joy and purpose tend to live longer.

# CHAPTER II

# THE EPIDEMIOLOGY OF AGING

When I was in medical school, the subject of epidemiology was considered boring compared to other specialties, such as internal medicine and neurosurgery, which were deemed more exciting and therefore more attractive. However, the onset of COVID-19 revealed geriatric epidemiology to be a critically important field, as older populations were disproportionately impacted during the pandemic.

As the world's population continues to age, it is vitally important to study the cause and occurrence of disease in this growing segment of the population. By 2030, one in six people on the planet will be aged 60 years or over. The number of persons aged 80 years or older is expected to triple between 2020 and 2050 to reach 426 million, according to the World Health Organization (WHO). In recognition of this reality, the United Nations established 2021-2030 as the Decade of Healthy Ageing, a global collaboration to transform attitudes toward aging and promote better healthcare solutions for older populations. Before discussing how to reach the goal of living healthily to 100, let's briefly review the statistics of life expectancy.

## 1 What is Aging? What is Life Expectancy?

Biologically speaking and as defined by the NIA, aging is identified as the time-related, progressive deterioration of physiological integrity leading to functional impairment and increased likelihood of death. At the molecular level, aging is an accumulation of chemical damage to the molecules inside our cells, which eventually affects the whole body.

From practical and legal perspectives, how is "old age" defined? Most developed countries set the retirement age at around 65 years old; this is also generally considered the transition from middle to old age. In the U.S., the eligibility mark for senior social programs is between 65 (Medicare) and 67 years old (Social Security, depending on your birth date). However, aging experts debate whether old age should be treated as a broad category or sub-categorized into different groups—for example, young-old (60-69), middle-old (70-79) and very old (80+). In many East

Asian and Southeast Asian countries, reaching the age of 60 has traditionally been an occasion to be celebrated because it represents a zodiac milestone (there are five zodiac phases—metal, fire, water, earth and wood—and each phase is 12 years long, with an animal assigned to each year. Twelve years x five phases = 60 years). But nowadays, the 60th birthday is not considered particularly special because so many so-called "young-old" people reach this milestone.

Life expectancy is usually defined as the average length of time that a person may expect to live. The life expectancy of various countries, using data from various sources including the U.S. Census Bureau, the WHO and the NIA, is listed below:

| | |
|---|---|
| **USA** | 79.11 |
| **Japan** | 85.29 |
| **South Korea** | 83.50 |
| **China** | 77.11 |
| **Germany** | 81.88 |

The improvement in life expectancy in most developed countries is due to reduced infant mortality, increased knowledge about diseases and their spread, and the use of vaccines and antibiotics, to name a few reasons. When I was growing up in Korea in the early 1950s, shortly after the country was liberated from 36 years of Japanese occupation, the life expectancy was around 41 years. Today, Koreans are expected to live a little over 82 years, a 100% increase in life expectancy. In the city of Daegu, I vividly remember seeing piles of bodies in the summer, victims of the raging cholera endemic taking place at the time. Tuberculosis, parasites and other acute and chronic infections also plagued the entire population back then. I myself was a victim of a roundworm parasite (*Ascaris*) belonging to the nematode phylum. (Ironically, another nematode, *C. elegans*, a millimeter-sized roundworm, is a valuable laboratory model in basic research because it has many types of cells packed into a relatively simple anatomy. Scientists used *C. elegans* for studying aging and genetic research, facilitating the discovery of microRNA.)

Over the years, all of these infectious diseases have been gradually eradicated and these days we have nonagenarians, or people living into their 90s. The United States' 90-and-older population nearly tripled from 1980 to 2010, reaching 1.9 million, according to a report by the U.S. Census Bureau's American Community Survey, and was projected to more than quadruple over the next four decades, comprising 9.9% of the population by 2050. Among the 90-and-older population, women outnumber men

by a ratio of nearly 3-to-1. Interestingly, more than 80% of women 90 and older are widowed, while more than 40% of men this age are married.

But with a rapidly aging population comes a host of age-related medical issues. Most people 90 and older report having one or more disabilities, including cognitive decline, cardiovascular disorders, kidney diseases and cancer. An older person's likelihood of living in a nursing home increases sharply with age.

Dr. Tom Perls is the founding director of the New England Centenarian Study, the largest study of people in their 100s in the United States. Perls found that centenarians and their children, who are typically in their 70s through 90s, age relatively slowly and have decreased risk for aging-related diseases including Alzheimer's, cancer and diabetes. Exceptional longevity can run strongly in families, but lifestyle factors have a far larger influence than genes. "About 25% of the variation in human longevity is due to genetic factors," wrote Giuseppe Passarino, Francesco De Rango and Alberto Montesanto in a 2016 paper in *Immunity & Ageing*. Adopting good habits such as maintaining a healthy diet and weight, exercising regularly, drinking alcohol in moderation and completely abstaining from tobacco products can significantly reduce premature mortality. A healthy lifestyle can add years to your life—up until about your mid-80s, when genetics matter more and more. It is still rare to live to 100, but the number of centenarians is increasing worldwide.

| Country | Estimated number of centenarians (year recorded) | Centenarians per 100,000 people |
|---|---|---|
| USA | 80,000 (2020) | 24.2 |
| Japan | 92,000 (2023) | 74.1 |
| S. Korea | 22,000 (2020) | 42.4 |
| China | 54,000 (2013) | 4.0 |
| Germany | 24,000 (2021) | 28.2 |

In 2015, the world was home to nearly half a million centenarians, more than four times as many than in 1990. The growth of this population is accelerating and is expected to reach 3.7 million across the globe in 2050. Japan and Italy will have the highest proportion of people in their 100s, while the number of centenarians will grow fastest in China, where the population is expected to age rapidly in the coming decades. In Japan, the number of people over 100 is highly skewed toward females, a ratio of 7-to-1. Many experts attribute Japan's high life expectancy to the Japanese

diet and hygienic practices. In Okinawa, studies have identified five factors that have contributed to the large number of centenarians in that region: diet, low stress, a caring community, high levels of physical activity and spirituality (for more details see Chapter V, section 2, “Diets”).

With life expectancy increasing, countries are implementing policies to encourage more births and to adjust to aging societies, especially in East Asia, where shrinking workforces will put a strain on economies and healthcare systems. Although at present, South Korea does not have pressing issues with an aging population, it will soon become an aging society as well. The country’s birth rate is the lowest in the world, and the government provides incentives to encourage the fertility rate. China has entered an era of negative population growth, a result of its one child policy implemented between 1980 and 2015. Like South Korea, China is also struggling with a low fertility rate, in part due to the economic hardship associated with raising children in a competitive society. Japan, a nation with one of the largest aging populations, is similarly struggling with a low birth rate, compounded by a longer life expectancy and a strict immigration policy.

The study of other animals provides some insight into the causes of aging. Life expectancy in the natural world varies widely, from insect life spans of a few days to hundreds of years for certain whales, sharks and giant tortoises. The maximum life span of humans is estimated to be 120 years, while that of our best friend, the domestic dog, is about 20 years. Laboratory rodents live about three to four years, while fruit flies live about three months.

Biologist Steven Austad at the University of Alabama first proposed the concept of a longevity quotient, LQ (akin to the intelligence quotient, IQ). LQ is the ratio of a species’ actual maximum longevity to the predicted maximum life span for its body mass. Mathematically, LQ is defined as the observed longevity divided by the expected longevity. Austad’s key insight was using body mass to arrive at the expected longevity. In general, larger animals tend to live longer relative to smaller animals. According to the LQ formulation, Austad characterizes mice as poor agers and identifies Greenland sharks (with a maximum longevity as long as 500 years), roughage rockfish (200 years) and salamanders (decades) as extraordinarily good agers. The LQ for humans, 5.1, is considered relatively good for mammals.

## 2 Blue Zones

In 2000, Michel Poulain, originally a trained astrophysicist who became a specialist in international migration statistics and longevity, introduced the concept of Blue Zones, areas where the population experiences exceptionally high longevity. These regions are:

- Nuoro Province, Sardinia, Italy
- Okinawa Prefecture, Japan
- Nicoya Peninsula, Costa Rica
- Icaria, Greece

Later, explorer and journalist Dan Buettner, in researching Blue Zones as a National Geographic Fellow, added a city in the U.S.: Loma Linda, Calif. He described its predominantly Seventh-day Adventist community as having unusual longevity due in part to a healthy lifestyle and plant-based diet. Loma Linda is only five miles from San Bernardino, the birthplace of the original McDonald's hamburger. The average lifespan of people living in San Bernardino is decades shorter compared to the lifespan of those living in Loma Linda.

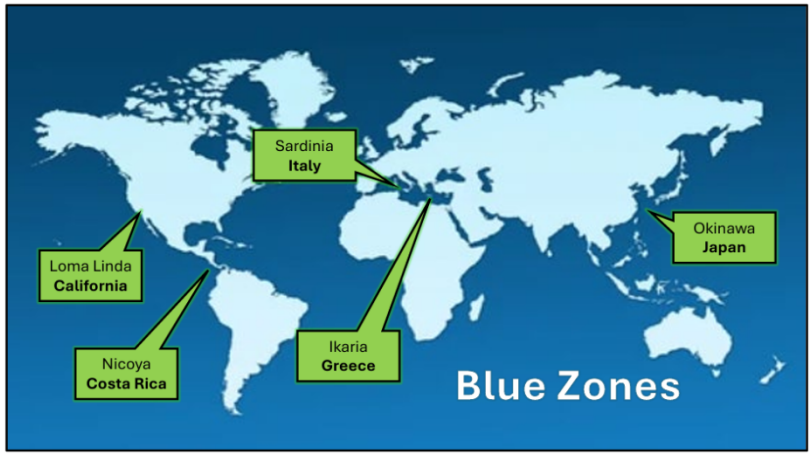


**Fig. 2-1** Blue Zones are areas of the world where people tend to live significantly longer and healthier lives. People who live in Blue Zones share common lifestyle factors that impact longevity such as healthy diets, regular physical activity, social engagement and a sense of purpose.

Recently, Buettner documented the characteristics of Blue Zone regions in a 2023 Netflix series titled *Live to 100: Secrets of the Blue Zones*. The longevity of Blue Zone populations apparently results from practicing a lifestyle that includes regular physical activity, having family and community support and consuming locally produced food. Regardless of location and population diversity, the same lifestyle characteristics were identified across all five Blue Zones, which Buettner termed the "Power 9" principles. They include:

- *Activity*: Move naturally. Walk every day.
- *Outlook*: Downshift. Reduce stress. Articulate a sense of purpose.
- *Diet*: Mostly plant-based including whole grains, greens, sweet potatoes, nuts and beans. Low on beef and dairy. Big on tea and red wine. Seventh-day Adventists in Loma Linda tend to abstain from caffeine.
- *80 Percent Rule*: Avoid overeating. Stop eating when feeling 80% full. Have a large breakfast and a smaller lunch. Dinner is the smallest meal of the day.
- *Connections*: Loved ones first. Belong to a faith-based community. Surround yourself with healthy people, as healthy behaviors are contagious.

Buettner has since founded the marketing company Blue Zones LLC and designated more Blue Zones in the U.S. The preliminary findings on documenting healthy lifestyles in these areas are encouraging.

## 3 Signs of Aging

When talking about signs of aging, one might picture wrinkled skin, silvery white hair, missing teeth and a stooped posture.

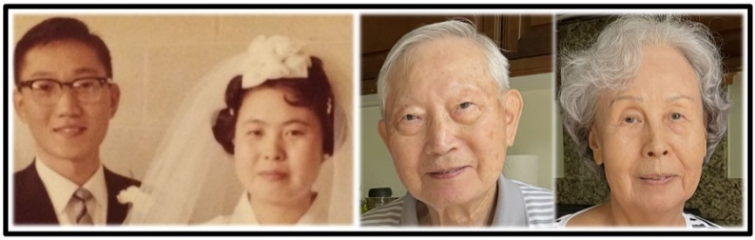

**Fig. 2-2** The author and his wife of 65-plus years in their youth (20s) and maturity (80s).

The aging process actually starts in the mid-30s. The following are some typical aging symptoms, although none are considered characteristic of a specific disease.

**Skin**: Collagen in the dermis production slows down after 40. Wrinkles form as fibers begin to break and stiffen. In addition, a decline in blood vessels leads to a decrease in circulation, causing loss of nutrients and making it more difficult for cells to regenerate. After excessive UV exposure, stem cells in keratinocytes (one of the skin cells in the epidermis) undergo what is called apoptosis, also known as cell suicide, resulting in cell death.

Other age-related skin disorders include dry skin, itching and bruises. Age spots, once called "liver spots," are flat, brown spots often caused by overexposure to the sun. Skin tags are small, typically flesh-colored growths of skin that have a raised surface. They are usually harmless.

More serious age-related skin disorders include three types of skin cancers. Two of those, basal cell carcinoma and squamous cell carcinoma, grow slowly and rarely spread to other parts of the body, traveling to the regional lymph nodes and other tissues. Local therapy is typically able to eradicate early stages of these cancers. The third and most dangerous type of skin cancer is malignant melanoma, which readily metastasizes to regional lymph nodes and distant organs. Surgery and immunotherapy are the mainstay therapies of melanoma. Early-stage melanoma is highly curable.

**Hair:** Hair graying and hair loss (alopecia) are frequently reported as among the first signs of aging and affect quality of life. Age-related hair loss is more prevalent in men than women (53% and 37%, respectively). Though genetics and hormones, particularly the male hormone known as dihydro-testosterone, play major roles in hair loss in men, the exact mechanisms aren't fully known. Despite the significant impact on quality of life and high demand for treatment, to date there are presently only two Food and Drug Administration (FDA)-approved medications available (topical or oral minoxidil, brand name Rogaine; and finasteride, also known as Propecia).

**Teeth:** Tooth enamel tends to wear away over time, making teeth vulnerable to damage and decay. Roots are more porous than crowns, which leads to tooth loss, as does dry mouth (a side effect of many prescription and over-the-counter medications) and gingivitis (inflammation of gums). Tooth loss is one of the major impacts on quality of life among older adults. Some dentists claim that gum disease in older people is a harbinger of age-related disorders. In January 2024, Dr. Jonathan An of the Universi-

ty of Washington's School of Dentistry received funding from the FDA to investigate whether the drug rapamycin might alleviate or prevent gum disease in older populations (see more in Chapter IV, section 3, "Pharmacological Approaches"). Another age-related oral disease is oral cancer. If detected early, oral cancers can be treated effectively.

**Vision**: Age-related macular degeneration (AMD) can develop initially as central vision compromise, resulting in a loss of vision. The likelihood of developing AMD increases with age, affecting nearly 12% of those above 80 years old. There are two types of AMD: Dry AMD is indolent, whereas wet AMD is progressive and results in loss of vision relatively quickly. New medications are available for the treatment of wet AMD. Other age-related eye disorders include diabetic retinopathy, glaucoma, dry eye, presbyopia and cataracts. Cataracts occur when the lens of the eye becomes cloudy, making vision blurry. Presbyopia results from weakness in the eye's ciliary muscle, an involuntary muscle that focuses the eye by changing the shape of the lens.

**Hearing**: Almost 50% of people older than 75 have hearing loss, initially losing high-pitched sounds. Age-related hearing loss, also called presbycusis, comes on gradually as a person grows older and usually affects both ears equally. It seems to run in families and may occur because of changes in the inner ear and auditory nerve, which relays signals from the ear to the brain. Because the loss is gradual, people with presbycusis may not realize they have lost some of their ability to hear. Hearing loss, even in small amounts, is linked to an increased risk for falls. Sometimes older people become depressed or withdrawn from others because they feel frustrated or embarrassed over not being able to hear what is being said. There may also be a connection between hearing loss and cognitive decline, since hearing loss often results in social withdrawal. Nowadays, hearing aids are available without a prescription.

**Bone and Muscle**: Aging represents the single greatest risk factor in skeletal fragility, including osteoporosis, especially in post-menopausal women. Based on data about bone mineral density (BMD) measurements taken at the femoral neck and lumbar spine as well as census data from 2005 to 2010, there are an estimated 10.2 million Americans with osteoporosis, and 54% (53.6 million) of U.S. adults aged 50 years and older have osteopenia, a precursor to the disease. Osteoporosis-related fractures are more common in women than men, and it is generally estimated that one in three women will suffer an osteoporotic fracture in her remaining lifetime. The National Osteoporosis Foundation recommends that women aged 65