Quest for Vitality & Immortality
Advances in Age Management

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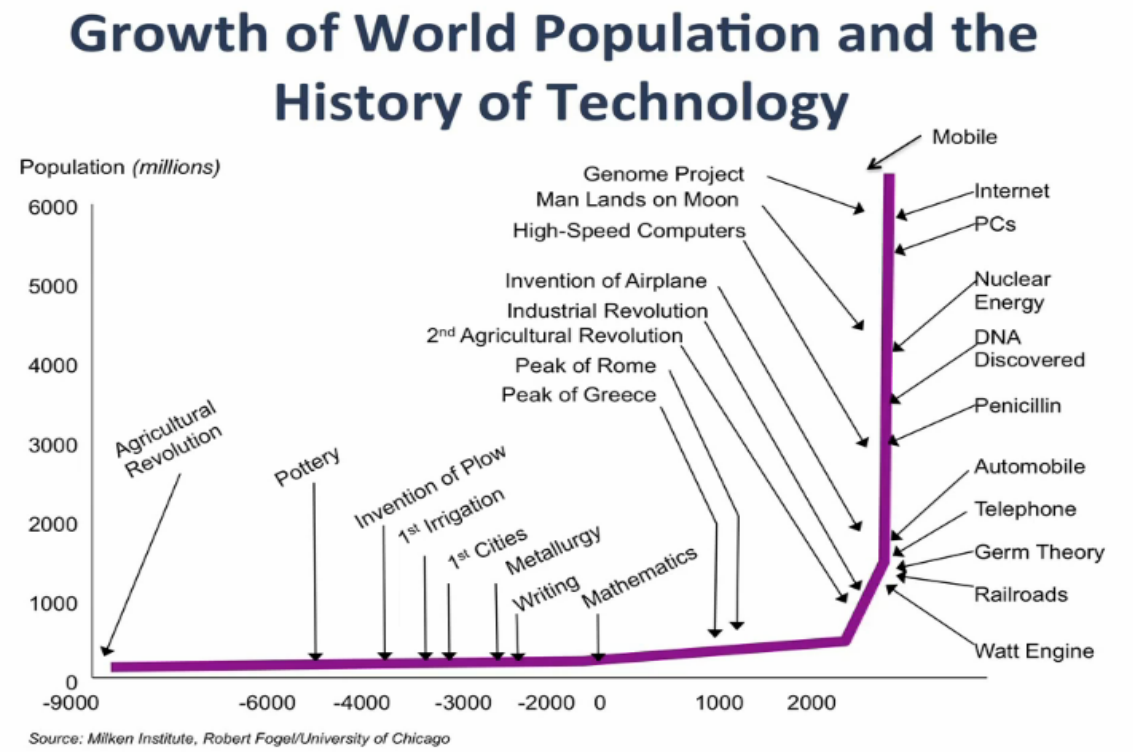
"I don't want to achieve immortality through my work. I want to achieve it through not dying." ~ Woody Allen

The timeline from the first flight to supersonic transport and the first rocket to a manned mission to the moon have been breathtakingly brief. The first theory that a chemical means of transmission of genetic information, to the identification of DNA, took a few years. The progress since then leading to new fields of genomics, epigenetics, gene sequencing, gene correction, and transfer has been nothing short of revolutionary. The life span of various rodents is remarkably varied, and even more varied are the lifespans of different animals. Some life forms have been identified that have lifespans measured in the thousands of years, others appear to be immortal. The Nobel Prize in Medicine was given to Dr. Sydney Brenner for his work on the genetics of the roundworm, which has parallels to the genomics of man. Modifying one single gene led to a near ten-fold increase in its lifespan, the human equivalent of reaching an age one thousand years. The single cell at fertilization, through replication and cell division, becomes over 37 trillion specialized cells in the adult. Each cell carries a duplicate of the DNA of its parent cells unless a mutation occurs. The power of exponential or logarithmic growth is often vastly underestimated. Human life expectancy has increased, predominantly through reductions in infant mortality.

Free radicals, oxidation, and inflammation and are the biological equivalent of rust and aging. Genes are not destiny; epigenetic influences from the environment modify genes as well as turning them on and off. Telomeres, the ends of the chromosomes that act as the equivalent of shoelace caplets, prevent the unraveling of DNA and cell death. The enzyme telomerase prevents the shortening of telomeres and enhances cell longevity. Cancer cells use telomerase to maintain cancer cell viability and propagation, making some cancer cell lines virtually immortal. Genetic mutations that trigger accelerated aging, such as progeria, are providing important insight into the mechanisms of aging that offers potential therapy to control the aging process. One of the control genes of aging found in the roundworm is also present in mouse and man. A metabolite of a microbe found in the soil of Easter Island influences this gene and leads to extended lifespan in the roundworm, and evidence of age reversal in mice. This compound is FDA

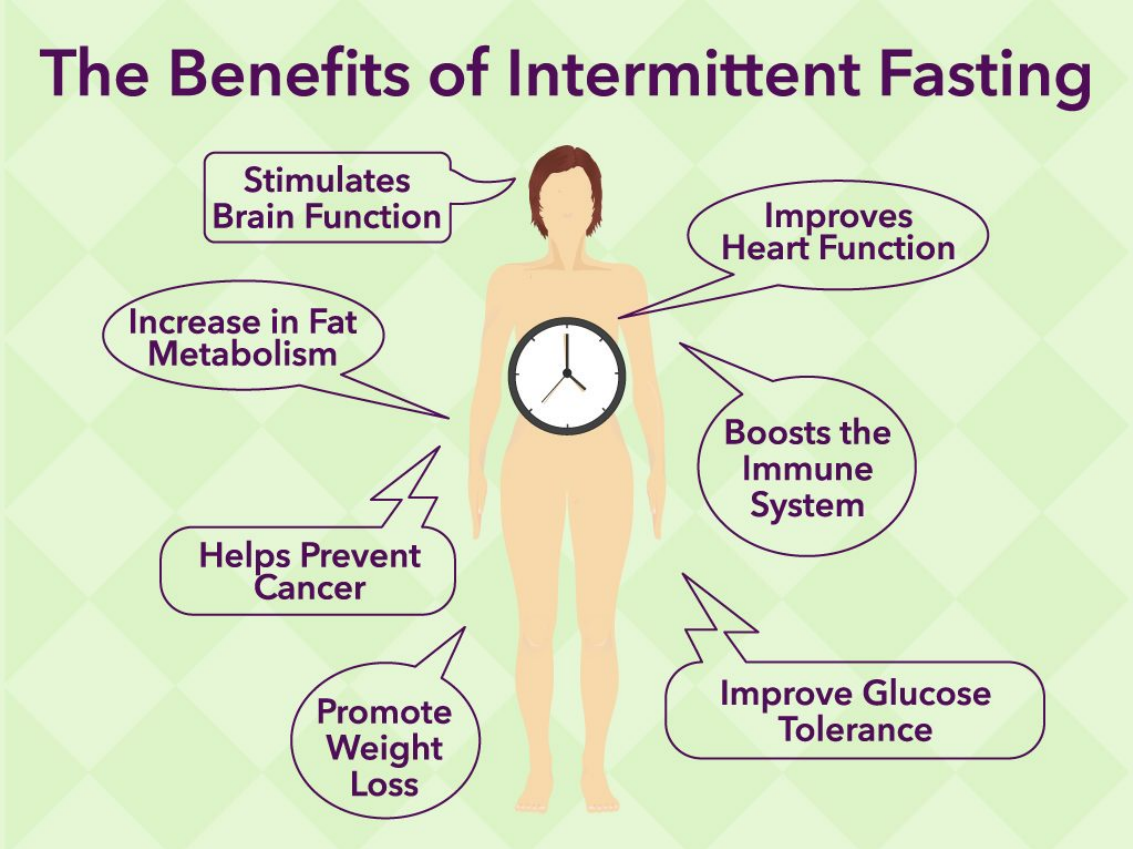
approved for treating post organ transplant patients to prevent rejection, and human trials to assess its effect on aging are ongoing. Laboratory advances in roundworms and mice are providing important insights, but applications in humans require extensive study, even if the sane genes are shared between species. The advent of new technology, such as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) has brought gene transfer and correction of genetic mutations from the world of science fiction to present day reality.



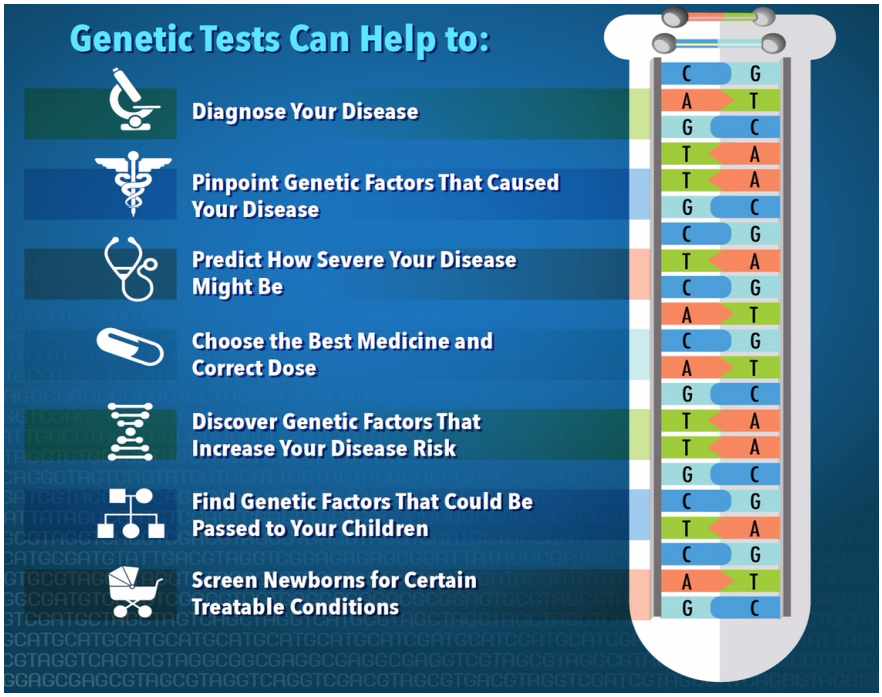
On occasion, the result of a new scientific advance meets or exceeds the initial hype. Stem cells are one example where the advances have rapidly moved from the laboratory to clinical applications. Stem cell therapy has moved from the laboratory to clinical applications relatively rapidly. The first stem cell transplant took place over fifty years ago with bone marrow transplants. The condition amenable to new approaches with stem cells is expanding rapidly. Organ regeneration and replacement, as well as cloning for organ retrieval, are no longer science fiction but on the horizon. Limb and organ regeneration from stem cells and gene transfers to correct mutations or provide new properties are within technological reach. The image of the glowing cat is an actual demonstration that the gene of the firefly can be transplanted into a completely different species, and function as it was designed to physiologically. The other images are fictional and humorous representations of what is theoretically possible if carried to the extreme. Advances in technology have made prosthetics that have similar or superior properties to the human original possible. Further advances will accelerate advances over the natural features, and even today the Olympics disallow blade runners who have a speeds advantage over normal limbs. Many of the diseases that result in death today, such as myocardial infarction and heart failure, are theoretically curable with a mechanical prosthetic heart or one regenerated from stem cells.

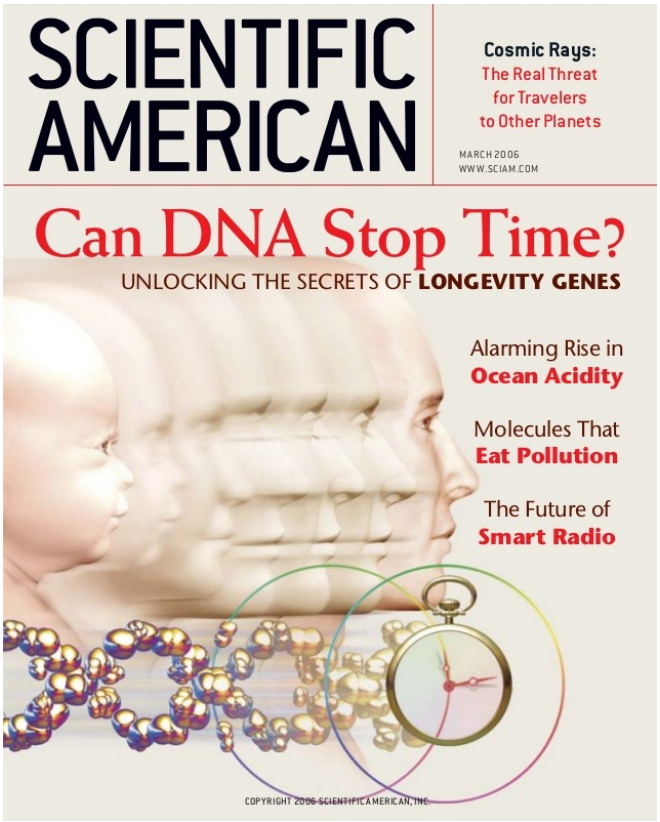
Nanotechnology is rapidly advancing, and an entirely new field of technology and medicine will offer remarkable diagnostic and therapeutic advances. Hormones were the original focus of aging and vitality research and continued to have an important role to play. Testosterone and growth hormone supplements are not without risks, and the science of longevity and age management is rapidly advancing beyond hormone therapy. Lifestyle, diet, stress, inflammation, and a variety of factors have been identified by studying centenarians, those who have lived a century or more, in ‘blue zone’ communities around the world where they are found in sizeable number. Caloric restriction extends lifespan in mice and other organisms. Some humans are adapting this approach, with the results unknown as yet.

Laboratory research has identified compounds that mimic the effect of caloric restriction, so it is possible that in the future you can literally have your cake and eat it too! Diet plays an important role in inflammation and its management. Many people believe inflammation should be referred to as inflamed-aging because of its profound effect on the aging process. Red wine and resveratrol have received a lot of publicity for anti-aging effects, but to date the results of resveratrol compounds have been disappointing. One of the lessons learned from the concept of systems biology is that individual components may require other factors to achieve results. So even though resveratrol by itself may not have proven benefits, perhaps when taken with other key components in the elixir of red wine, it is beneficial. The Mediterranean diet, as well as the red wine industry, suggests this is the correct path to take, in moderation of course.



Without a doubt, exercise appears to have the greatest anti-aging effects known to date. Perhaps one day the benefit will be available in pill form, but even then you should take the pill for a long walk each day before swallowing it! The diet we consume undoubtedly is another key to our health and longevity. It may have a direct influence by its components, or indirect via changes in epigenetics and the microbiome. Even when the diet appeared to play a direct role, such as fat content and cardiovascular risk, the truth was much more complicated. For example, phosphatidylcholine is a vital phospholipid substance found in every cell of the human body. As it was first identified in eggs it was given the name lecithin derived from the Greek word lekithos (λεκιθος, egg yolk). The Western diet is rich in lecithin, which the gut microbes use to create trimethylamine, which is then absorbed by the gut and converted by the liver to TMAO. Choline, betaine, and trimethylamine N-oxide (TMAO) are metabolites of lecithin and are associated with cardiovascular risk in humans. TMAO has been associated with accelerated atherosclerosis, enhanced playlet hyper-reactivity, and thrombosis risk. Vegetarian, vegan, and Mediterranean diets (dairy, eggs, legumes, vegetables, seafood) are associated with lower TMAO levels. Gut microbial suppression with antibiotics reduces plasma levels of TMAO. Who would have imagined that the food was influenced by the microbiome, and then metabolized by the liver, and then could affect the cardiovascular system?



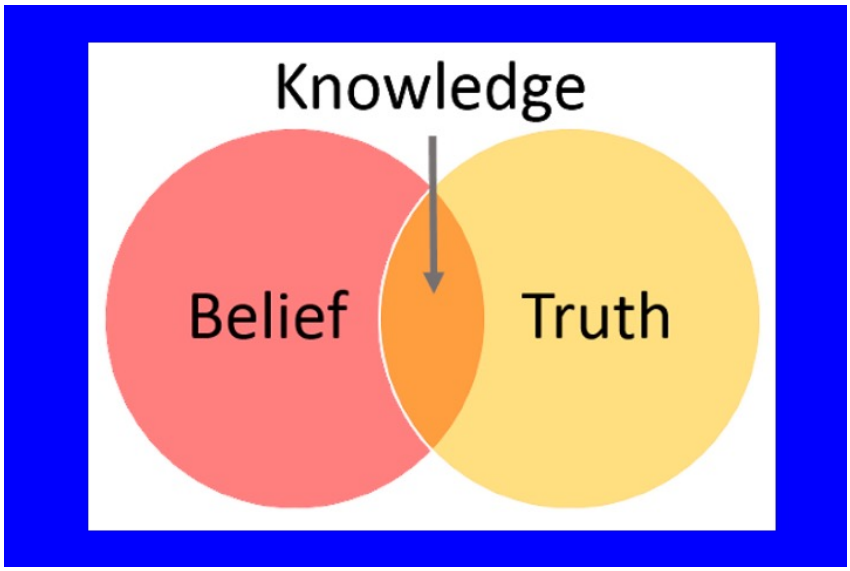


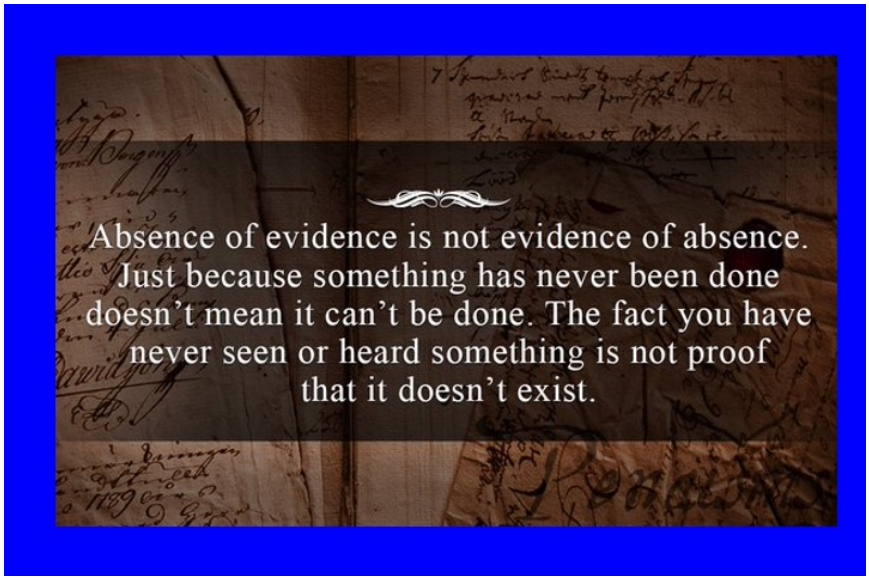
The human microbiome and its genes have a profound influence on human health. We are constantly exposed to new organisms, and the microbiome is always adapting. The use of probiotics, antibiotics, prebiotics, dietary supplements, nutraceuticals, prescription and over the counter drugs can affect the microbiome in so many ways that the consequences cannot be predicted with certainty. What can be predicted is that they will be heavily marketed and promoted because there is a huge profit to be made, and safety and efficacy are secondary afterthoughts. Sometimes the wisdom of sages past cannot be improved upon, this is one of them. Some cancers, such as breast and colon, can be identified early when highly curable. Surveillance for those at higher risk is suggested. Further advances in genomics may identify populations at risk, and blood tests may replace the screening tests we use today. Colon cancer

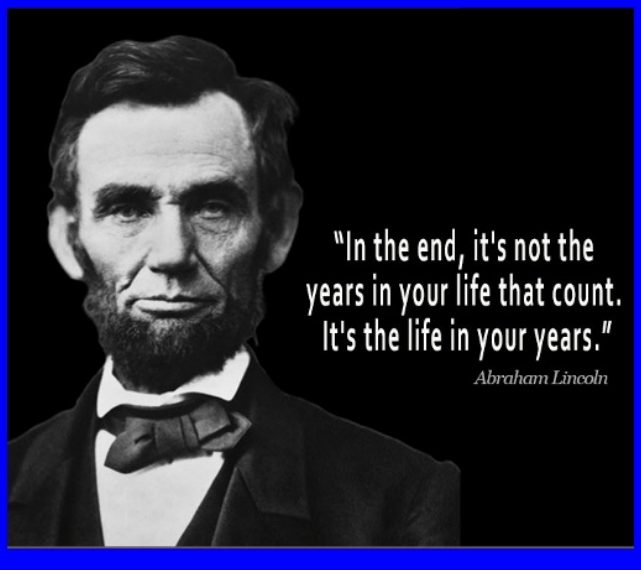
screening is suggested for those over fifty years of age, and for younger individuals who have a history or family history of colon cancer, colon polyps, inflammatory bowel disease, and specific genetic markers.

Colonoscopy has been the 'gold standard', but new options include capsule colonoscopy, a high-tech image transmitter that is swallowed and sends images for review. The latest FDA-approved test was a fecal (stool) DNA test for markers of colon cancer and polyps. Technology and approaches are changing, but getting screened may well be a lifesaver, as these cancers often do not exhibit signs or symptoms until they are no longer curable. Freezing the whole body, or just the head, for hopeful revitalization has a market and a rationale, but a whole host of obstacles make the technological feasibility of returning in the future uncertain. Personalized medicine, utilizing genomics and other technology, is the future of medicine. The 'one size fits all' approach to population-based medicine has been a disaster that the public is, for the most part, unaware of.

The cover of Time magazine prophesizing 2045 as the year man becomes immortal is based on the concept of singularity, downloading your consciousness and brain onto a computer cyborg equivalent. This will probably become an option, to have a virtual life and existence, with equally complex moral and social choices. The possibility of becoming an electronic mind reminds me of a cartoon image of a janitor unplugging a complex life support technology to plug in his floor polisher.







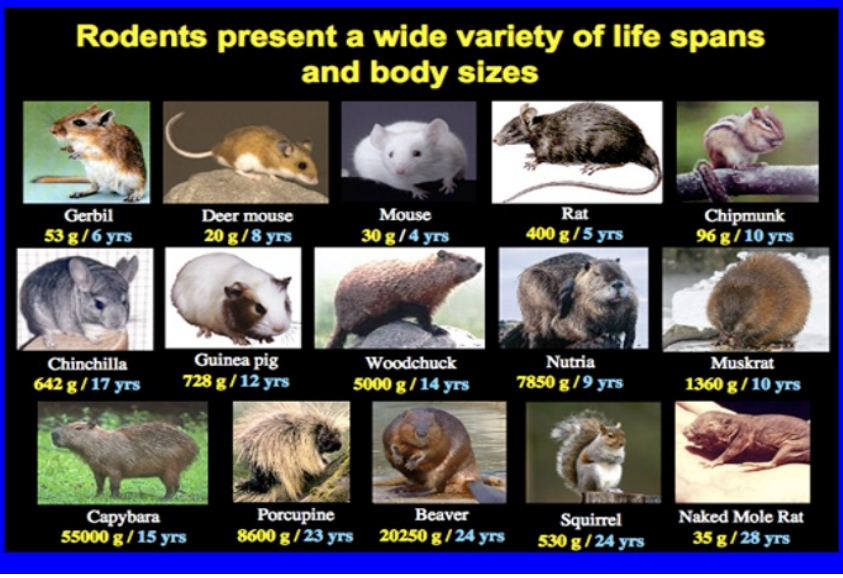
And the pace of change is unprecedented

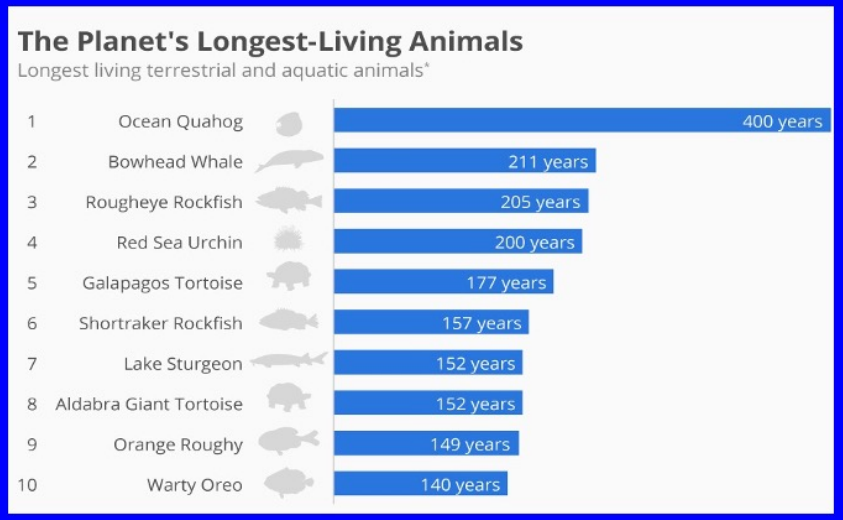
Knowledge Doubling Curve

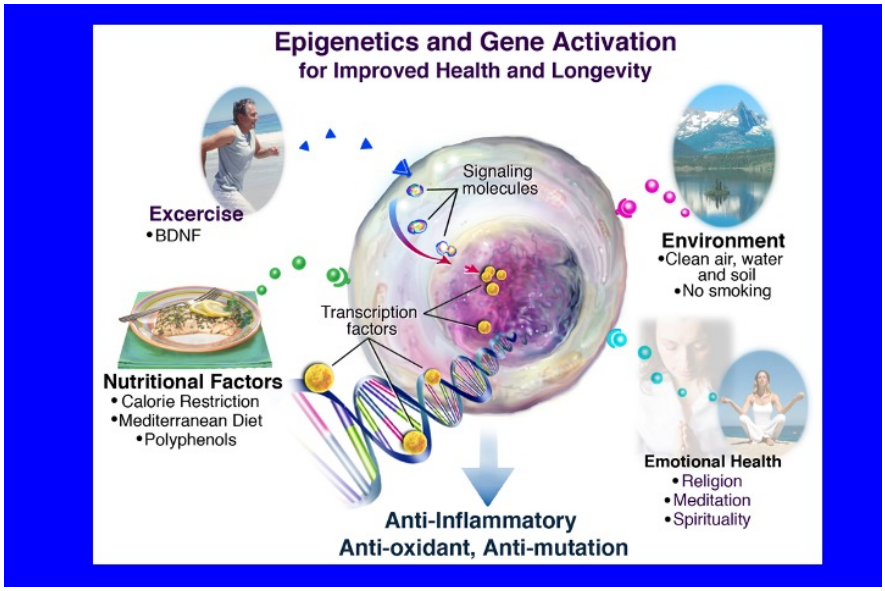
- 1900s, Knowledge doubled every century
- 1940s, knowledge doubled every 25 years
- Currently, knowledge doubling every 13 months
- Soon, every 12 hours?

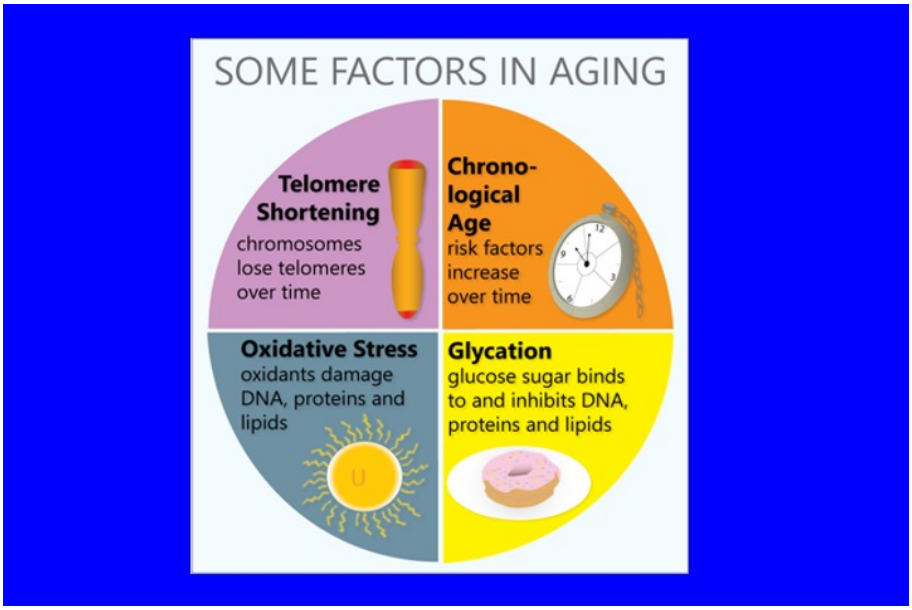
'Transition from the linear growth to exponential growth of human knowledge has taken place.'

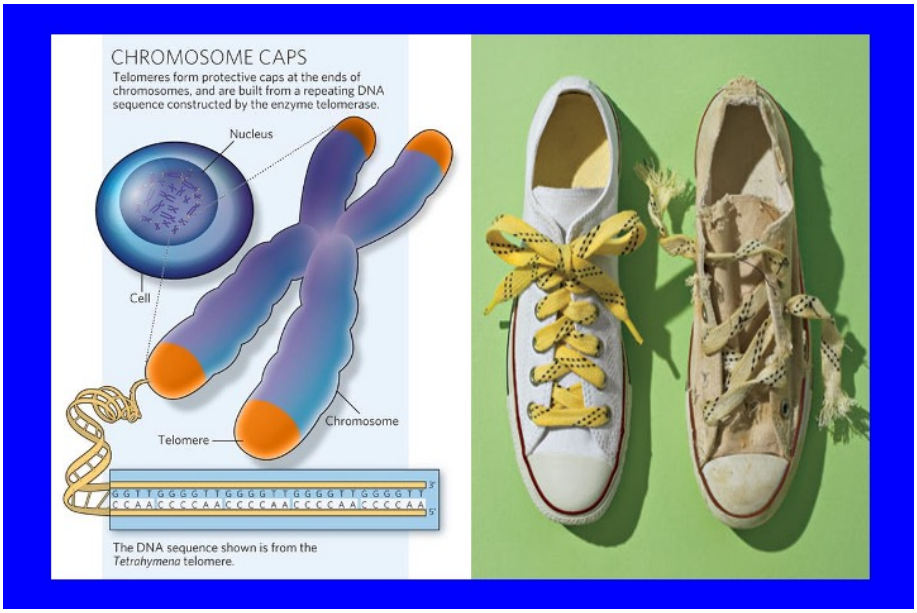
Source: Buckminster Fuller and IBM, Harvard University Jeff Lichtman
http://www.futuristgerd.com/2014/07/16/knowledge-doubling-every-12-months-soon-to-be-every-12-hours-via-industry-tap/

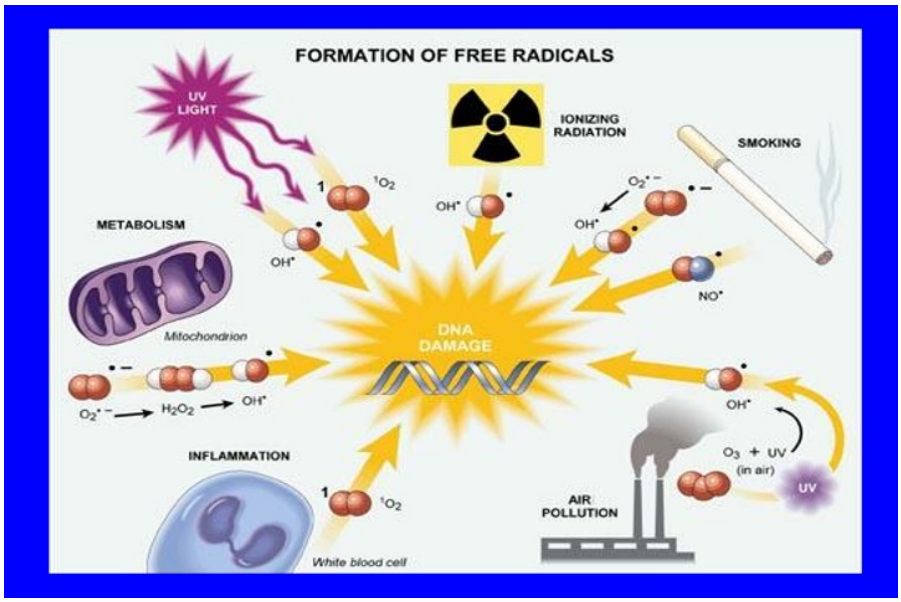

Rodents present a wide variety of life spans and body sizes
Gerbil
53 g / 6 yrs
Deer mouse
20 g / 8 yrs
Mouse
30 g / 4 yrs
Rat
400 g / 5 yrs
Chipmunk
96 g / 10 yrs
Chinchilla
642 g / 17 yrs
Guinea pig
728 g / 12 yrs
Woodchuck
5000 g / 14 yrs
Nutria
7850 g / 9 yrs
Muskrat
1360 g / 10 yrs
Capybara
55000 g / 15 yrs
Porcupine
8600 g / 23 yrs
Beaver
20250 g / 24 yrs
Squirrel
530 g / 24 yrs
Naked Mole Rat
35 g / 28 yrs

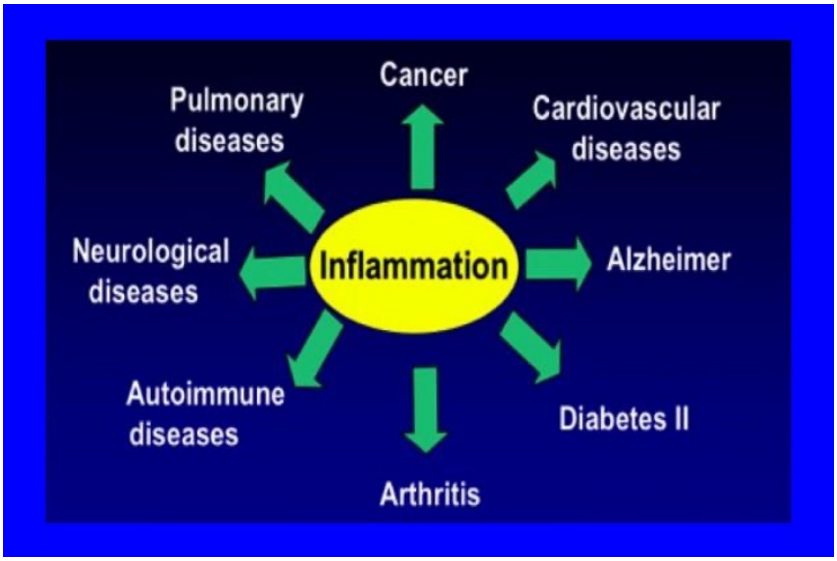

The Planet's Longest-Living Animals
Longest living terrestrial and aquatic animals*
1 Ocean Quahog 400 years
2 Bowhead Whale 211 years
3 Rougheye Rockfish 205 years
4 Red Sea Urchin 200 years
5 Galapagos Tortoise 177 years
6 Shortraker Rockfish 157 years
7 Lake Sturgeon 152 years
8 Aldabra Giant Tortoise 152 years
9 Orange Roughy 149 years
10 Warty Oreo 140 years


Epigenetics and Gene Activation
for Improved Health and Longevity
Excercise
•BDNF
Signaling molecules
Environment
•Clean air, water and soil
•No smoking
Transcription factors
Nutritional Factors
• Calorie Restriction
•Mediterranean Diet
•Polyphenols
Emotional Health
• Religion
• Meditation
• Spirituality
Anti-Inflammatory
Anti-oxidant, Anti-mutation


SOME FACTORS IN AGING
Telomere Shortening
chromosomes lose telomeres over time
Chrono-logical Age
risk factors increase over time
Oxidative Stress
oxidants damage DNA, proteins and lipids
Glycation
glucose sugar binds to and inhibits DNA, proteins and lipids

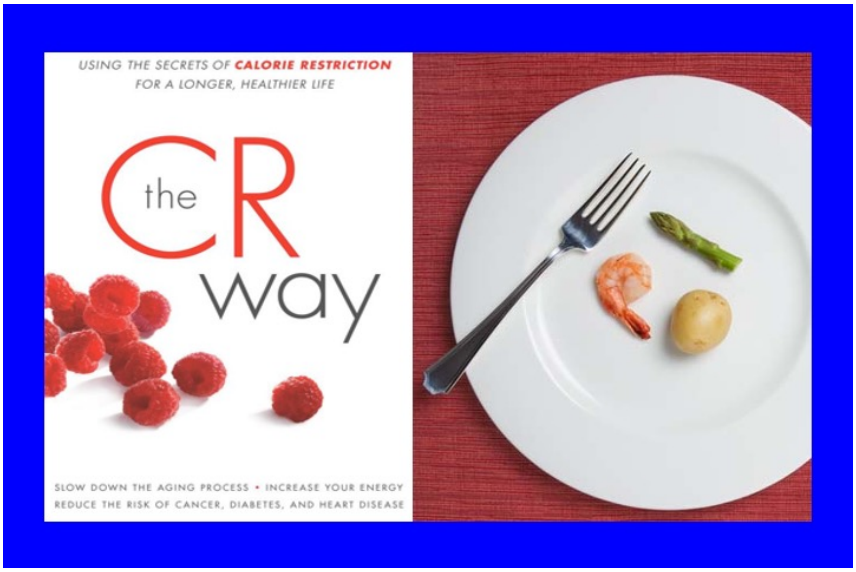

CHROMOSOME CAPS
Telomeres form protective caps at the ends of chromosomes, and are built from a repeating DNA sequence constructed by the enzyme telomerase.
Nucleus
Cell
Chromosome
Telomere
The DNA sequence shown is from the Tetrahymena telomere.


FORMATION OF FREE RADICALS
UV LIGHT
IONIZING RADIATION
SMOKING
METABOLISM
Mitochondrion
DNA DAMAGE
INFLAMMATION
White blood cell
AIR POLLUTION
UV



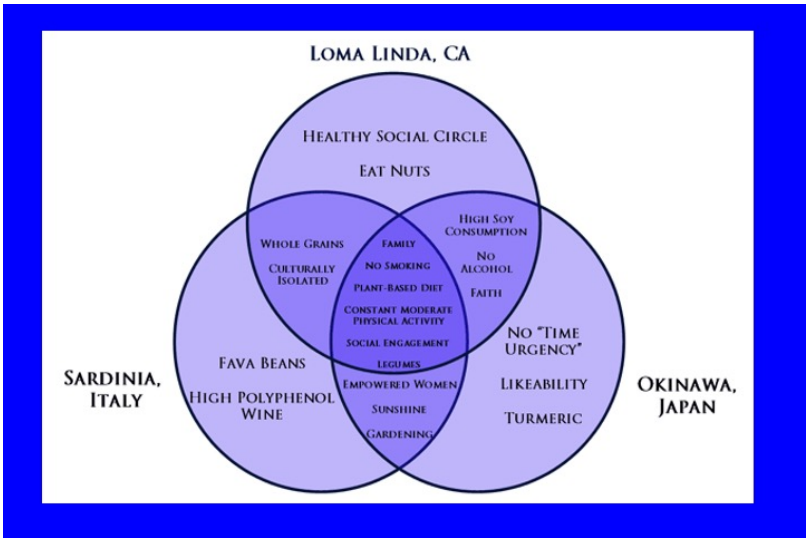
Examples of Phytochemicals and Their Food Source

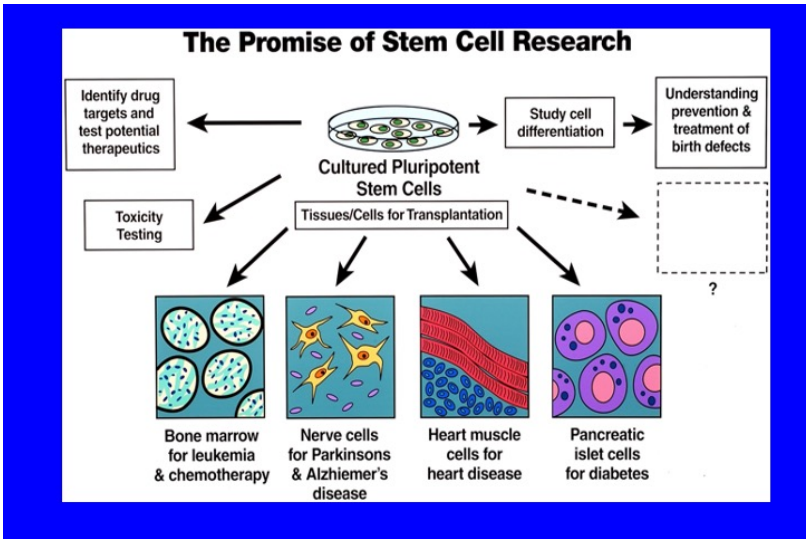
Class (Subclass)	Phytochemical	Food Source
Carotenoids (Carotenes)	Beta-Carotene, Lycopene	Carrots, dark leafy greens (spinach), tomatoes
Carotenoids (Triterpenoid)	Saponins	Soybeans, beans, other legumes, corn, alfalfa
Polyphenols (Curcuminoids)	Curcumin	Turmeric, mustard
Polyphenols (Flavonoids)	Quercetin	Cranberries, apples, red and yellow onions, beans
Polyphenols (Isoflavonoid)	Isoflavones (phytoestrogens)	Soybeans, alfalfa sprouts, chickpeas, peanuts
Polyphenols (Stilbenoids)	Resveratrol	Grape skins and seeds, nuts, peanuts

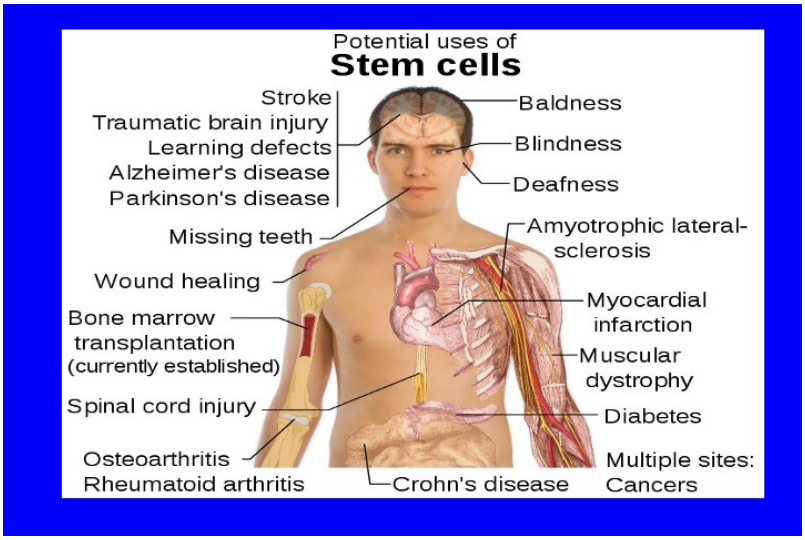

USING THE SECRETS OF CALORIE RESTRICTION
FOR A LONGER, HEALTHIER LIFE
the CR way
SLOW DOWN THE AGING PROCESS • INCREASE YOUR ENERGY
REDUCE THE RISK OF CANCER, DIABETES, AND HEART DISEASE


5 Types of Fasting
Simple Fast: 12 hours
Cycle Fast: 16 hours - 3x weekly
Strong Fast: 16-18 hours daily
Warrior Fast: 19-21 hours daily
1 Day Fast: Full 24 hour fast each week


LOMA LINDA
CALIFORNIA
NICOYA
COSTA RICA
SARDINIA
ITALY
ICARIA
GREECE
OKINAWA
JAPAN
BLUE ZONES
LONGEVITY HOTSPOTS
BLUE ZONE LIFE LESSONS
MOVE NATURALLY
RIGHT TRIBE
RIGHT OUTLOOK
EAT WISELY

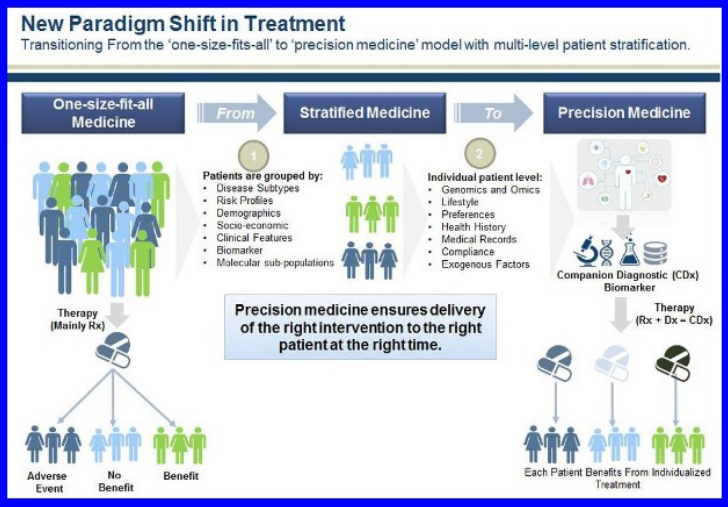

LOMA LINDA, CA
HEALTHY SOCIAL CIRCLE
EAT NUTS
WHOLE GRAINS
CULTURALLY ISOLATED
FAMILY
NO SMOKING
PLANT-BASED DIET
CONSTANT MODERATE PHYSICAL ACTIVITY
SOCIAL ENGAGEMENT
LEGUMES
EMPOWERED WOMEN
SUNSHINE
GARDENING
HIGH SOY CONSUMPTION
NO ALCOHOL
FAITH
NO "TIME URGENCY"
LIKEABILITY
TURMERIC
SARDINIA, ITALY
FAVA BEANS
HIGH POLYPHENOL WINE
OKINAWA, JAPAN


The Promise of Stem Cell Research
Identify drug targets and test potential therapeutics
Cultured Pluripotent Stem Cells
Study cell differentiation
Understanding prevention & treatment of birth defects
Toxicity Testing
Tissues/Cells for Transplantation
?
Bone marrow for leukemia & chemotherapy
Nerve cells for Parkinsons & Alzhiemer's disease
Heart muscle cells for heart disease
Pancreatic islet cells for diabetes


Potential uses of
Stem cells
Stroke
Traumatic brain injury
Learning defects
Alzheimer's disease
Parkinson's disease
Baldness
Blindness
Deafness
Missing teeth
Amyotrophic lateral-sclerosis
Wound healing
Myocardial infarction
Bone marrow transplantation (currently established)
Muscular dystrophy
Spinal cord injury
Diabetes
Osteoarthritis
Rheumatoid arthritis
Crohn's disease
Multiple sites: Cancers

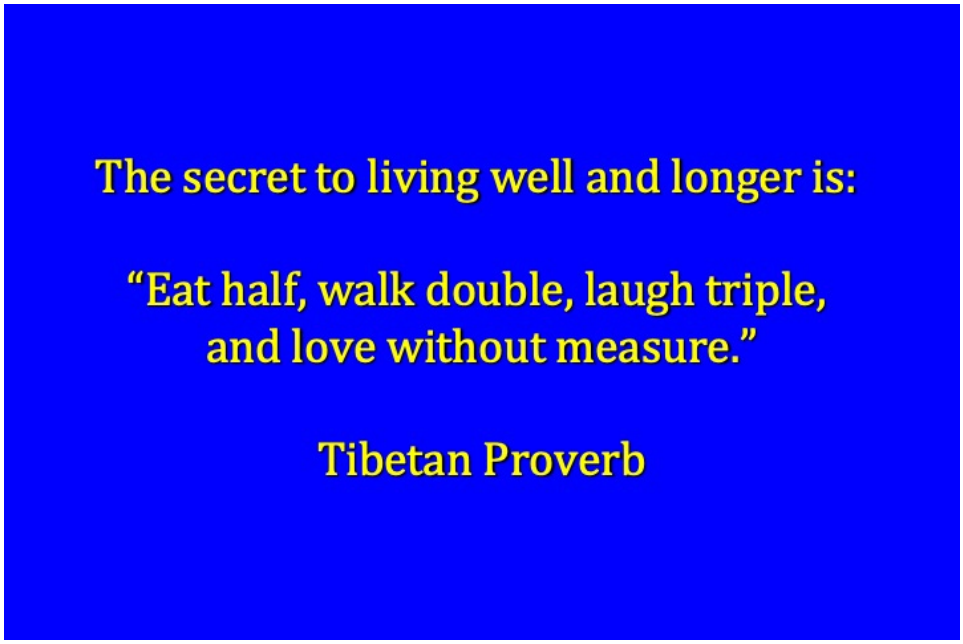
Regenerative Medicine: Definition

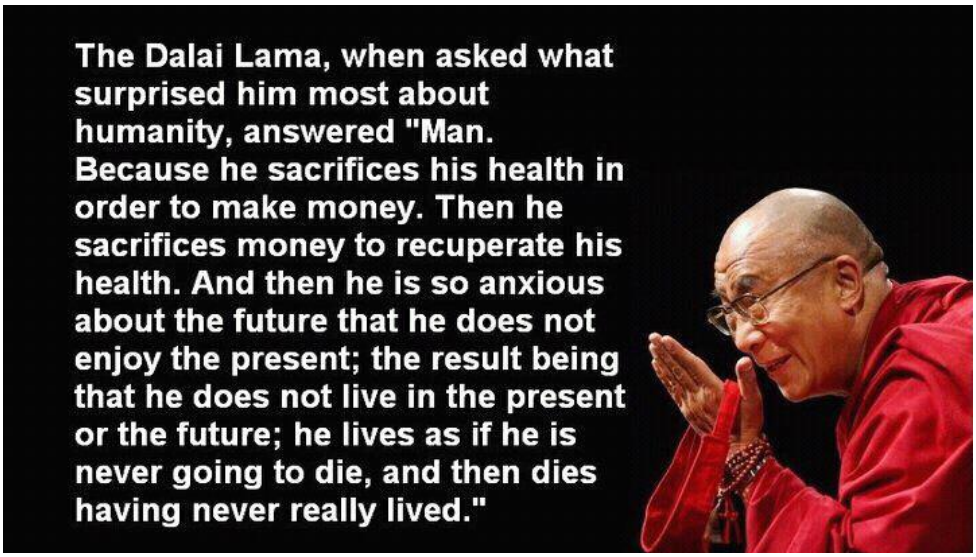
- 'Regenerative medicine replaces or regenerates human cells, tissue or organs, to restore or establish normal function.'[1] Includes different types of therapies. For instance[2]:
  - Stem cell therapy
  - Cellular therapy
  - Tissue engineering
  - Gene therapy (sits between stem cell and cellular therapy)
- Regenerative medicine has the potential to "deliver new, innovative therapies, or even **cures**, where conventional approaches do not provide adequate solutions[3]



Tips for Living Younger Longer

- Exercise body & mind, flexibility, and balance
- Mediterranean pesco-vegetarian diet, antioxidants
- Preventive, personalized, precision health care
- Proactive stress reduction, enhance immunity
- Social activity with friends and family
- Meditation, practice of belief
- Reduce tobacco, alcohol, sitting is the new smoking
- Enjoy and experience all of your senses including purpose, empathy, gratitude, humor, and common sense





References:

1) vB Hjelmborg J, Iachine I, Skytthe A, et al. Genetic influence on human lifespan and longevity. Hum Genet 2006; 119:312.
2) Artz A. From biology to clinical practice: aging and hematopoietic cell transplantation. Biol Blood Marrow Transplant 2012; 18
3) Kim S, Jazwinski S. The Gut Microbiota and Healthy Aging: A Mini-Review. Gerontology 2018; 64:513.
4) Ragonnaud E, Biragyn A. Gut microbiota as the key controllers of "healthy" aging of elderly people. Immun Ageing 2021; 18:2.
5) Petralia R, Mattson M, Yao P. "Aging and longevity in the simplest animals and the quest for immortality". Ageing Res Rev. 2014;**16**: 66–82.
6) Rando T, Chang HY "Aging, rejuvenation, and epigenetic reprogramming: resetting the aging clock". Cell 2012; **148** (1–2): 46–57.
7) Sebastiani P, Gurinovich A, Bae H, et al. Four genome-wide association studies identify new extreme longevity variants. J Gerontol A Biol Sci Med Sci. 2017 Oct 12;72(11):1453-1464.

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Joseph B. Weiss, M.D. is Clinical Professor of Medicine in the Division of Gastroenterology, Department of Medicine, at the University of California, San Diego. Accepted to university at age fifteen he attended the University of Michigan, University of Detroit, and Wayne State University. Reflecting his broad interests, he majored in Medieval English Literature, Astrophysics, and Invertebrate Zoology. Following his graduation from the Wayne State University School of Medicine in Detroit, Michigan, he completed his internship and residency in Internal Medicine at the University of California, Irvine Medical Center in Orange, California. Under the auspices of the World Health Organization and others, he has pursued interests in Tropical and International Medicine and Public Health with extended stays in Africa, the Middle East, and Latin America. Subsequently completing a clinical and research fellowship in Gastroenterology at the University of California, San Diego, he has remained active on the clinical faculty of the School of Medicine. Dr. Weiss is a Fellow of the American College of Physicians, a Fellow of the American Gastroenterological Association, and a Senior Fellow of the American College of Gastroenterology. Double board certified in Internal Medicine and Gastroenterology, Dr. Weiss has over thirty years of clinical, administrative, and research experience. He has also served on the Board of Directors of the Scripps Clinic Medical Group, Clinical Board of Governors of the Scripps Clinic and Research Foundation, and Chancellor's Associates of the University of California, San Diego

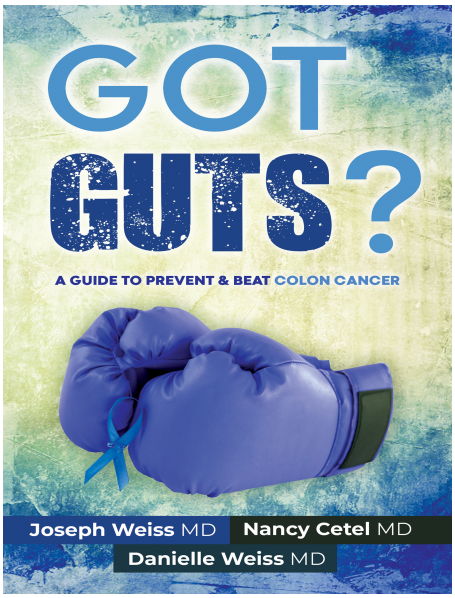
He is the author of more than a dozen books on health (www.smartaskbooks.com) and has had numerous papers published in prestigious national and international medical journals, as well as in the lay press. Dr. Weiss is also an accomplished humorist and professional speaker having given over three thousand presentations nationally and internationally. He has presented at international conferences and conventions, universities, medical schools, hospitals and medical centers, Fortune 500 companies, YPO/WPO, Bohemian Grove, Esalen Institute, Renaissance Weekend, Aspen Brain Forum, IDEA World Convention, international destination spas & resorts (Golden Door, Canyon Ranch, Rancho La Puerta), etc.

The programs offered are continuously updated with cutting edge information. Well-spoken, enlightening, and entertaining the programs are also visually engaging. Frequently requested programs include To 'Air' is Human (intestinal gas), The Quest for Immortality (longevity & vitality), The Scoop on Poop (gut microbiome & scatology), Digest on Digestion (digestive health & nutrition), Medical WisDumb (marketing hype to health advances), Laughter (& Chocolate) is the Best Medicine (humor in health & wellness), Food for Thought (brain-gut-microbiome axis) and others. For further information, contact Dr. Weiss at speakingofhealth@gmail.com or weisscme@ucsd.edu

These colorful, informative, and entertaining volumes are available at www.smartaskbooks.com, Amazon.com, BarnesandNoble.com, and major booksellers.

"Dr. Joseph Weiss' books provide an informative and entertaining approach to sharing insights about our digestive system and wellbeing." ***Deepak Chopra, MD***

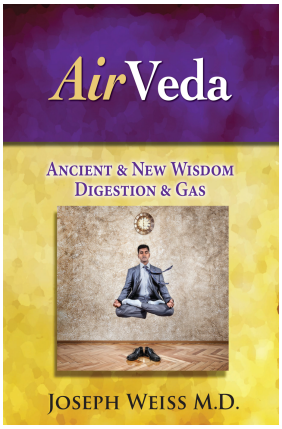
"Joseph Weiss, M.D. has a gift for books that are uniquely informative and entertaining. **Jack Canfield**
Coauthor of the Chicken Soup for the Soul® series

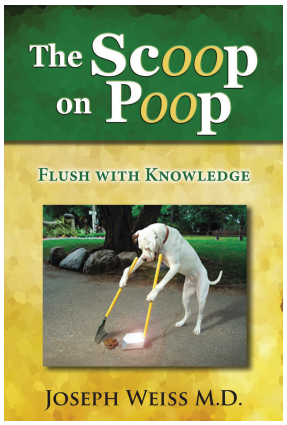


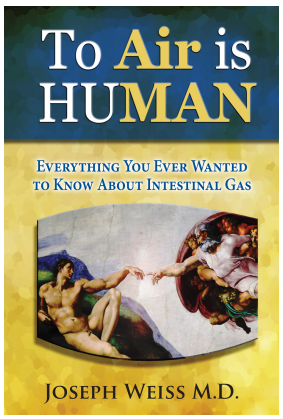
Got Guts! A Guide to Prevent & Beat Colon Cancer (ISBN:978-1-943760-97-8 Color Pages: 146 Words: 60,935 Images: 15) offers a clear understanding of the importance and value of prevention and screening in colorectal cancer. Written for the general public, it is a practical common-sense guide. Colon cancer is one of the most common and deadly cancers. It is both preventable and curable when found early, but devastating when discovered too late. It begins silently without any signs or symptoms, and rarely gives any warning until too late. In spite of painless, accurate and inexpensive screening tests, too many people mistakenly believe they are safe and fail to protect themselves.

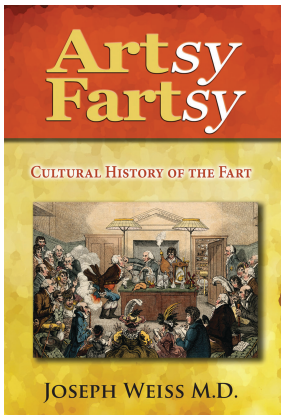
From young movie stars and professional athletes, to world political and religious leaders anyone can get colon cancer. Nearly 50,000 needlessly die in the United States each year from this preventable and curable disease. When it is detected early nearly all of these lives could have been saved. Recently the greatest increase in colon cancer is seen in adults 18 to 49 years of age. In this book you will learn how: your diet, weight, family history, gender, and other significant factors contribute to your potential risk. You will begin to understand the essentials in personalizing your best approach to prevent colon cancer. The multiple options range from one minute painless and inexpensive tests, to the more involved invasive colonoscopy tests that require sedation or anesthesia. Understanding the options available , and selecting wisely based on your personal risk factors, is clearly explained in this potentially lifesaving book.

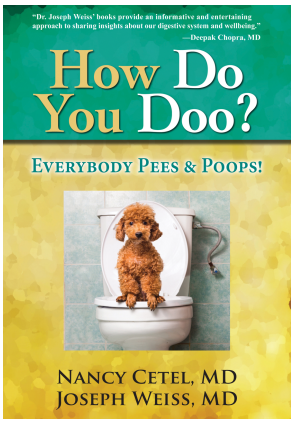
Written by expert physicians who offer an unbiased and logical approach, *Got Guts!* assists in identifying your best path. This guide may well be the most important book you will read to protect your health now and in the future. All three authors have experienced the hardships that follow a loved one diagnosed with colorectal cancer too late. They are dedicated and compassionate physicians with extensive clinical, academic, and research experience. Don't miss an opportunity to make life-saving decisions for yourself and your loved ones!











The Scoop on Poop! Flush with Knowledge (ISBN: 978-1-943760-00-8 Color Pages: 426 Words: 111,763 Images: 378) is a uniquely informative tastefully entertaining, and well-illustrated volume that is full of it! The 'it' being a comprehensive and knowledgeable overview of all topics related to the remains of the digestive process. It has been provocatively and cheekily retitled as ***You Don't Know Sh*t! Until You Read This Book*** (ISBN: 978-1-943760-04-6 Color Pages: 426 Words: 111,768 Images: 378). Whether you disdain it or appreciate it, it is part of the human (and animal) experience. The purpose of this volume is to share rarely discussed but very important knowledge about the important role of digestion and the gut microbiome in human health and wellness

AirVeda: Ancient & New Wisdom, Digestion & Gas (ISBN: 978-1-943760-10-7 Color Pages: 467 Words: 150,062 Images: 399) covers the remarkable advances in the understanding of digestive health and wellness from Ayurveda to genomics and the gut-brain-microbiome-diet axis. The knowledge gained opens new avenues to optimal health and wellness.

To 'Air' is Human, Everything You Ever Wanted to Know About Intestinal Gas (ISBN: 978-1-943760-02-2 Color Pages: 321 Words: 92,567 Images: 297) covers everything you ever wanted to know about the burp, belch, bloat, fart and everything digestive but were either too afraid or too embarrassed to ask. This volume is overflowing with practical information, fascinating facts, surprising trivia, and tasteful humorous insight about this universal phenomenon. https://www.amazon.com/Air-Human-Everything-Wanted-Intestinal/dp/1943760020

Artsy Fartsy, Cultural History of the Fart (ISBN: 978-1-943760-03-9 Color Pages: 322 Words: 79,364 Images: 266) is a fascinating and colorful review of the fart through human culture and history. A cough, sneeze, hiccup, stomach rumble, burp, belch, and other bodily sounds simply cannot compete with the notoriety of the fart. Whether encountered live and in person or through the medium of literature, television, film, art, or music it may leave a powerful and lingering memory.

How Do You Doo? Everybody Pees & Poops! (ISBN: 978-1-943760-06-0 Color Pages: 88 Words: 17,844 Images: 61) A delightfully informative, entertaining, and colorfully illustrated volume with valuable practical insights on toilet training. Tasteful color photographs and illustrations of animals answering the call of nature allows the child to understand that everybody does it! Additional informative relevant content to entertain the adult while the child is 'on the potty' is included.