HOW TO LIVE TO BE A 100

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OBJECTIVES

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  1) Review the causes of a shortened life
  2) Review the effective steps to prevent disease
  3) Review theories of aging in disease free life extension

"Age to me means nothing. I can't get old; I'm working. I was old when I was twenty-one and out of work. As long as you're working, you stay young. When I'm in front of an audience, all that love and vitality sweeps over me and I forget my age."

"If you ask what is the single most important key to longevity, I would have to say it is avoiding worry, stress and tension. And if you didn't ask me, I'd still have to say it."

"If you live to be one hundred, you've got it made. Very few people die past that age."

"You can't help getting older, but you don't have to get old."

"You know you're getting old when you stoop to tie your shoelaces and wonder what else you could do while you're down there."

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A **centenarian** is a person who has attained the age of **100 years** or more.

A **supercentenarian** is a person who has lived to the age of **110** or more.

There are as many as **184,000 people** in the United States who are **100 years** of age or older.

**Long life is possible!**

**Supercentenarians**

Supercentenarian, Jeanne Calment, is considered to be the oldest person ever recorded at age 122.

On the islands of Okinawa, Japan there is a group that is among the longest lived on Earth.

In Sardinia, Italy there is a hot spot of longevity in mountain villages where men reach the age 100 at an unusual rate.

In Loma Linda, CA there are a group of Seventh-Day Adventists who rank among America’s longevity “all-stars.”

Residents of these 3 places produce a high rate of centenarians, suffer a fraction of the diseases that commonly kill people in other parts of the developed world, and enjoy more healthy years of life.

www.grg.org
We observe a steady rise from [1980 to 2000] in the amount of Supercentenarians over the last 25 years.

The numbers of US Centenarians are expected to rise exponentially between now and 2050.

Live to 100 – The Key Issues

- Identify and cure existing diseases which shorten life
- Prevent disease in the first place – “Primary Prevention”
- Slow or prevent aging
Causes of Premature Death

- Heart disease and Stroke (Atherosclerotic Vascular Disease and arterial thrombosis)
- Cancer
- Alzheimer’s Disease

Alzheimer’s Disease

- Current estimates suggest that by 2030 there will be 63 million people with dementia worldwide
- The prevalence of AD approaches 50% in those older than 90
- Hypertension is the major player in the pathogenesis of stroke, post stroke dementia, and vascular dementia (VAD)
- Alzheimer’s disease is the most common cause of dementia, contributing from 45% to >75% of the cases in Asians and whites

PREVENTION
QUESTION 1

Estrogen replacement therapy protects against Alzheimer's Disease
a) True
b) False

Atherosclerotic Vascular Disease: Vascular Disease Status

- Global risk factors

  - Obesity
  - Diabetes
  - Dyslipidemia
  - Hypertension
  - Smoking
  - Age
  - Sex
  - Family History
  - Previous MI
  - Thrombotic Factors

ASVD Prevention

- LDL lowering, HDL increase and modification (Apo-1 Milano)
- Prevention of inflammation
- Prevention of thrombosis
- Manage/Cure Diabetes Mellitus
- Control BP
- Normalize weight
- Exercise regularly
- Stop smoking
Apo A-1 Milano

- Based on the evidence provided by these various studies from Cedars-Sinai and additional confirmatory studies from Dr. Cesare Sirtori’s laboratory in Milan, Esperion Therapeutics initiated human trials of recombinant apo A-1 Milan
- In the small Phase 2 study, investigators showed that as in animal studies reported from Dr. Shah’s lab, once a week intravenous administration of recombinant apo A-1 Milano (ETC-216) for five weeks led to a significant and measurable shrinkage of human coronary artery plaques as measured by intravascular ultrasound technique
- These findings are unprecedented in that reversal of plaque size has been shown in five short weeks

http://www.csms.edu

Cancer Prevention

- Avoid carcinogens
- Consume diet high in antioxidants, isoflavones and fiber
- Immunize against infection-caused malignancy (HPV, Hepatitis B and C)
- Normalize body weight
- Avoid cancer-associated hormones such as Estrogen

Earlier researchers have shown that fruits like pomegranate are rich in antioxidant and anti-inflammatory activity and are effective against tumors in mouse skin. Pomegranate juice has very high antioxidant property and appears promising as an inhibitor agent. Several ecological studies suggest that sunlight may protect against prostate, colon, rectal, female breast, and ovarian cancer, all diseases that contribute to a substantially high proportion of cancer mortality in the Western industrialized world. Some analytical studies also suggest a protective association between circulating vitamin D in blood, which is largely derived from sunlight or dietary vitamin D, and colorectal and prostate cancer.

Epigallocatechin-3-gallate (ECCG), an abundant polyphenol found in green tea, potently inhibits vascular endothelial growth factor receptor-2, a key receptor involved in tumor angiogenesis. Oral infusion of polyphenolic fraction isolated from green tea at about 6 cups of green tea per day strongly inhibits development of prostate cancer.

J Cancer Res Ther, 2007
Cancer Prevention

Studies have consistently linked abundant consumption of plant-based food to a substantial reduction in risk of developing various cancers.

Laboratory studies show that this chemoprotective effect is related to the high levels of numerous phytochemicals in this food, which interfere with several cellular processes involved in the progression of cancer and also with inflammatory processes that foster development of cancer.

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Beliveau, Can Fam Phys 2007;53:1905-1911

Alzheimer's Disease Prevention

For the primary prevention of Alzheimer’s disease there is good evidence for controlling vascular risk factors.

There is weak or insufficient evidence for prescribing of medications.

Screening for the apolipoprotein E genotype in asymptomatic individuals in the general population is not recommended.

In the WHI Memory Study that enrolled participants from WHI, women taking estrogen were more likely to have dementia at follow-up than those in the placebo group after 4 years of follow-up. Zandi et al. found that earlier use of HRT for at least 10 years was associated with reduced risk of AD, suggesting that HRT plays a role in reducing risk of AD if used during menopause.

Evidence suggests NSAIDs offer some protection against AD when taken long-term, but there are no results from RCTs establishing efficacy for prevention of AD, and the appropriate dose, durations of use, starting age, and appropriate population remain unclear.

There is insufficient evidence to recommend vitamin E in treatment or prevention of AD.

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GINKGO BILOBA

The most recent studies have inconsistent results in support of the use of Ginkgo biloba in the treatment of dementia and there are serious side effects such as coma, bleeding, and seizures.

ESTROGEN

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The prevalence of obesity is on the increase all over the world.

Obesity is related to vascular diseases, and there is increasing evidence linking vascular risk factors to dementia and AD.

Obesity at midlife is associated with an increased risk of dementia and AD later in life. Clustering of vascular risk factors increases the risk in an additive manner. The role of weight reduction for the prevention of dementia needs to be further investigated.

Resveratrol

Resveratrol, trans-3,5,4'-trihydroxy-trans-stilbene is a phytoalexin produced by plants, and the skin of red grapes is rich in resveratrol which affects the processes underlying all three stages of carcinogenesis: tumor initiation, promotion, and progression. It has also been shown to suppress angiogenesis and metastasis. Extensive data in human cell cultures indicate that resveratrol can modulate multiple pathways involved in cell growth, apoptosis, and inflammation. The anti-carcinogenic effects of resveratrol appear to be closely associated with its antioxidant activity.

Several epidemiological studies indicate that moderate consumption of wine is associated with a lower incidence of Alzheimer’s disease.

Wine is enriched with antioxidant compounds with potential neuroprotective activities.

The exact molecular mechanisms involved in the beneficial effects of wine intake on the neurodegenerative process in Alzheimer’s disease remain unclear.

Marambaud et al., J Bio Chem 2005;280(45):37377-37382
Resveratrol

- **Resveratrol** markedly lowers the levels of secreted and intracellular amyloid-β peptides produced from different cell lines
- **Resveratrol** does not inhibit Aβ production because it has no effect on the Aβ-producing enzymes β- and γ-secretases, but instead promotes intracellular degradation of Aβ via a mechanism that involves the proteasome
- A proteasome-dependent anti-amyloidogenic activity of **resveratrol** is demonstrated and suggest that this natural compound has a therapeutic potential in Alzheimer’s disease

Marambaud et al., J Bio Chem 2005;280(45):37377-37382

The Biology of Aging

- Theories of aging can be divided into two general categories:
  1) stochastic
  2) developmental-genetic
- Increasing evidence suggests that aging may be the price we pay to avoid cancer
- The maximum lifespan potential may have been achieved due to our ability to grow old


Socioeconomic status and nutritional status have been strongly associated with life expectancy.

By 1900, improved sanitation helped to raise the average life expectancy in the US to 57 years, but infectious disease was still a major killer.

The increase in the average life expectancy has resulted in a compression of morbidity toward the end of this lifespan.

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The Biology of Aging

Telomere Biology and ASVD

What are Telomeres?
- A sequence of repetitive bases at the ends of linear chromosomes that prevent adjacent chromosomes from attaching to each other.
- Crucial to maintaining chromosome stability

Human Telomere Sequence

5'...TTAGGG TTAGGG TTAGGG TTAGGG TTAGGG TTAGGG..3'
3'...AATCCC AATCCC AATCCC AATCCC AATCCC AATCCC..5'


Telomeres and Aging

Studies suggest that lifespan could be increased 5 years by increasing the length of telomeres in people with shorter ones.

Geneticist Richard Cawthon believes that 10 to 30 years may be added to our lifespan by completely stopping telomere shortening.

www.learn.genetics.utah.edu
Vessels subjected to higher atherogenic hemodynamic stress

HUMAN STUDIES

ARTERIAL TISSUE

Greater age-related telomere shortening

WBCs

ARTERIAL TISSUE

Shorter telomere length and senescent phenotype

VSMCs

Shorter telomere length and senescent phenotype in fibrous cap

Patients with atherosclerotic disease (coronary, carotid, iliac artery)

ARTERIAL TISSUE

Shorter telomere length and senescent phenotype

WHAT CAN WE DO?

Geneticist Richard Cawthon

"If telomerase makes cancer cells (amortiff, is it prevent normal cells from aging?)"

"Could we extend lifespan by preserving or restoring the length of telomeres with telomerase? If we, does this raise a risk the telomerase also will cause cancer?"

"If all processes of aging could be eliminated and oxidative stress damage could be repaired, one estimate is people could live 1,000 years and they would die from causes like accidents, suicide, murder and pneumonia and some other infectious diseases."

Diet and Longevity

**CALORIE RESTRICTION**

In research studies, people practicing calorie restriction ate 20-25% less than their bodies needed. For example, a person who needs 2,000 daily calories for weight maintenance might eat 1,500 to 1,600 calories a day on a calorie restriction diet. People who follow a calorie restriction diet do so in hopes of slowing the aging process and extending their lives.

Short trials of calorie restriction diets in people have shown some benefit. People have seen positive changes in their:
- blood pressure
- blood sugar
- body fat percentage
- cholesterol levels
- heart rate
- weight

Despite the benefits, research has shown risks of calorie restriction diets, including:
- reduced bone density
- loss of muscle mass
- anemia
- memory loss
- dizziness
- depression

**BREAD, CEREAL, RICE & PASTA GROUP**

6-11 servings

**VEGETABLE GROUP**

3-5 servings

**FRUIT GROUP**

2-4 servings

**MEAT, POULTRY, FISH, DRY BEANS, EGGS & NUTS GROUP**

2-3 servings

**MILK, YOGURT & CHEESE GROUP**

2-3 servings

**FATS, OILS & SWEETS**

USE SPARINGLY

1992 USDA Food Guide Pyramid

**FATS, OILS & SWEETS**

USE SPARINGLY

**FATS, OILS & SWEETS**

USE SPARINGLY

2001 Harvard Medical School Guide to Healthy Eating
Agree or Disagree?

I exercise at least 40 minutes approximately 5 days a week

a) Agree
b) Disagree

Exercise and Longevity

Physical activity protects against the development of CHD, stroke, hypertension, obesity, non-insulin-dependent diabetes, and some cancers

Recent studies have suggested that at least one hour of walking a week predicted lower risk in people at high risk for CHD

Physical exercise improved functional capacity, enhances mood, thought, and psychological behavior and delays the infirmities and disabilities of old age

Paffenbarger RS, Int J Epidem 2001;30:1184-1192

I consume alcohol to protect against aging?

a) True
b) False
Alcohol and Longevity

Light to moderate alcohol consumption was associated with significantly lower rates of cardiac events and longer survival, independent of its anti-inflammatory effect.

Maraldi, Arch Intern Med 2006;166:1490-1497

Sleep and Longevity

“To age successfully, you must get a good night’s sleep. The greatest human longevity is found among those who average 7 to 8 hours of sleep a night.” - Edward Schneider, MD

“Sleep can in fact serve as a good indicator of a person’s longevity. Those who sleep lesser hours are more prone to dying sooner. A person needs a minimum of five hours of sleep a day in order to restore his/her physiological functions.” - Jacob Levin, MD

“Losing sleep can increase your stress hormone levels, interfere with your metabolism and cause memory problems. Lack of sleep can cause a variety of ailments ranging from loss of energy to depression. Chronic sleep deprivation can compromise your immune system and make you more susceptible to infections.” - Sonia Ancoli-Israel, MD

Stress and Longevity

• A new study suggests psychological stress may be enough to age a woman’s chromosomes by 10 years
• The link between stress, aging and health at the cellular level is unclear, but a team led by Elissa Epel of UC San Francisco has looked at the effect of stress on the cell
Stress and Longevity

Objective: to study the effect of stress on cells

Methods: Epel and her colleagues looked at the chromosomes in the white blood cells of 58 mothers, two-thirds of whom had chronically ill children

Results: There was no difference found in the telomere length of the two groups, but women in both groups who reported the most stress did have the shortest telomeres. The effect was so large that it represented nine to 17 years’ worth of cell aging

Conclusion: Stress affects us at the cellular level

www.newscientist.com

Anti-Aging Quackery

Anti-aging quackery are pervasive on the Internet and in clinics advertising anti-aging treatments

Anti-aging clinics thrive by administering human growth hormone (HGH) to thousands of gullible and vulnerable patients

Anti-aging quackery has become a multi-million dollar industry

Perls TT. J Geron 2004;59A(7):682-691

“Don’t look back. Something might be gaining on you.”

“Avoid fried meats, which angry up the blood.”

“If your stomach disputes you, lie down and pacify it with cool thoughts.”

“Avoid running at all times.”

“Go very light on the vices, such as carrying on in society; the social ramble ain’t restful.”

“Age is a question of mind over matter. If you don’t mind, it doesn’t matter.”

LeRoy (Satchel) Paige the great baseball pitcher
Formula for Longevity

EAT HEALTHY
EXERCISE YOUR BODY AND MIND
AVOID CARCINOGENS
GET GOOD SLEEP
STAY STRESS-FREE
STATE-OF-THE-ART TREATMENT FOR DISEASES