Age Management Medicine Prepares Us for Super Longevity

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Mission Statement

Age Management Medicine: Optimize human Healthspan and Lifespan to attempt to reach the maximum human potential of 115 years.

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Medical Director of the Age Management Institute

-Undergraduate and Graduate degrees in Biology, East Carolina University

-Graduate of Wake Forest University Bowman Gray School of Medicine

-Board Certified in Emergency Medicine

-Board Certified in Anti-Aging Medicine

-Past Assistant Professor UNR School of Medicine

-Certified in Age Management by Cenegenics Medical Institute

Age Management Medicine

- Based on peer reviewed medical literature.
- can add decades of vital lifespan with current technology.
- drastically slows down aging in motivated patients
- stay biologically young in preparation of future advances in longevity.

Brief review and current topics in Age Management

- Review of Age Management Medicine
- Thoughts on aging
- The major hormones keep us young
- Longevity genes

-strategies to activate sirtuins-drugs, fasting, exercise, supplements

Rudman Article New England Journal of Medicine 1990

- 6 month study of effects of Human Growth Hormone on men, average age 68
- Result:
  - Increase in Bone mineral density
  - Increase in lean muscle mass
  - Decrease in fat mass
  - Authors noted men appeared to be 10 to 15 years younger physiologically
  - Landmark article

Rudman Article-Continued

- This study was the first that led some doctors and scientists to start thinking about aging in a new light
- HGH study with men for 6 months showed improvements in muscle mass, bone density, and reduced fat.
- Led some scientists and physicians to look at aging as a disease model.

How was Anti-Aging or Age Management Medicine started?

- The American Academy of Anti-Aging Medicine was started in 1993
- 12 doctors and scientists
- Fastest growing new medical specialty worldwide
- Doctors, scientists, patients looking for a newer paradigm

Traditional Medicine

- Looks at aging as normal, do not treat.
- Treats the outcomes of disease
- Based on a fix-it-when-it's-broke model
- We are prisoners of our genetic destiny
- State of the art in acute trauma or acute medical crises
- Therapy biased heavily toward a surgical or pharmacological approach toward disease.

Age Management medicine (AMM)

- Aging is a disease
- We can change the process of aging.
- We are not prisoners of our genetic destiny
- Advanced preventative medicine
- Attempts to slow or prevent/reverse chronic disease
- Paradigm shift

Age Management Medicine Evaluation :Baseline data

- Screen adult patients for baseline data:

  -Dexa Scan for bone health-hips, spine, total bone score-compares bone mineral density to a 30 year old. Screen for osteopenia, osteoporosis.

  -Coronary CT-Calcium plaque scoring-identifies higher risk patients quickly. Ranges from zero to 5000+.

  -Body composition by DEXA scan: goals men < 20% body fat, measures visceral fat, women <25% body fat.

AMM baseline data: continued

- Comprehensive traditional and modern lab work

-Hgb A1C-diabetic risk with insulin levels, glucose monitoring also

-homocysteine-optimize if elevated (MTHFR)

-C-reactive protein-inflammatory marker Goal is < 1.0

Evaluation for AMM continued

- Baseline HGH levels-measure IGF-1
- Measure male and female hormones-Testosterone, estradiol, DHEA
- Vitamin D

Goal of AMM is to optimize health to a robust 30 year old

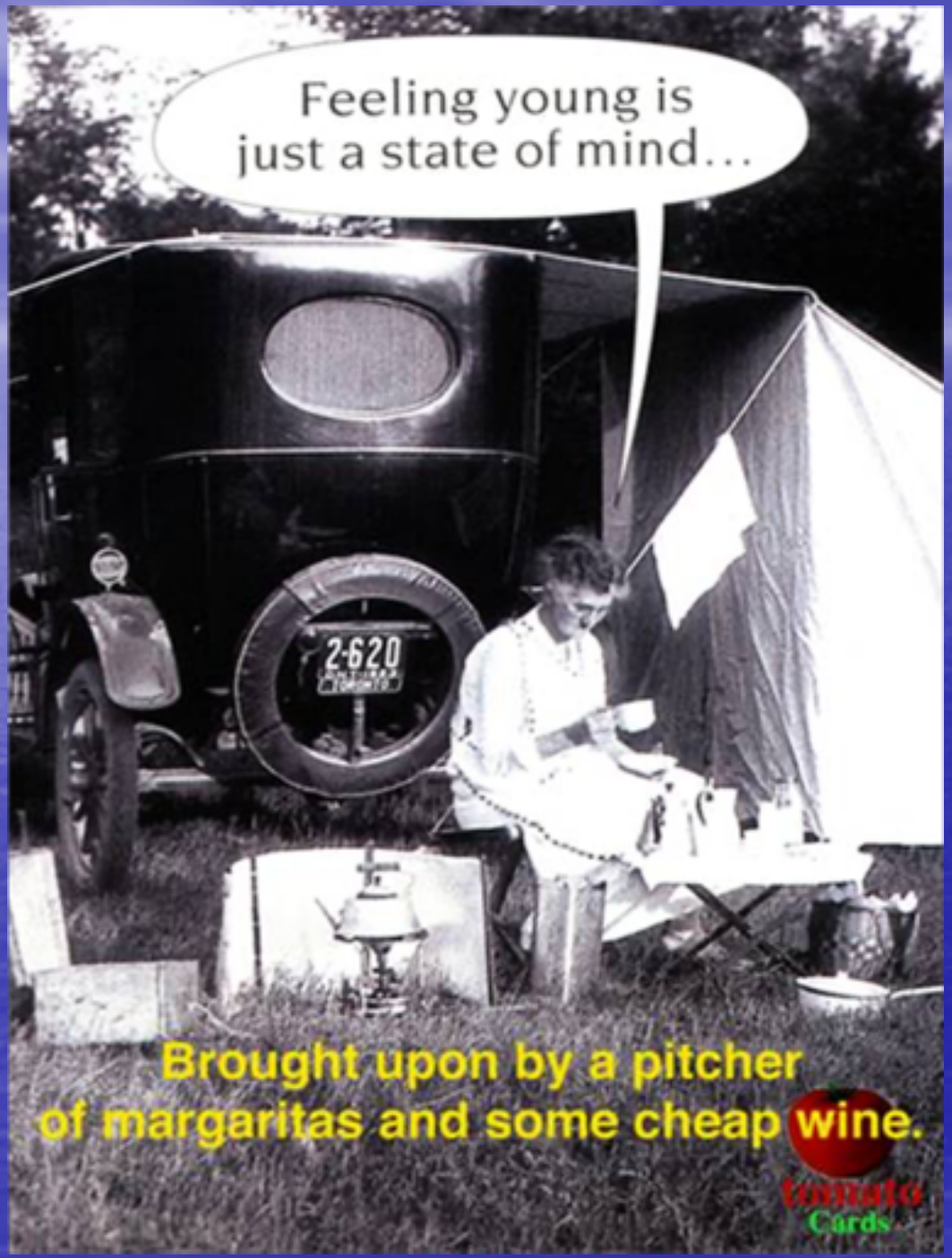
- Optimize frame (bones), body composition, restore major hormones if needed, modern diet , fasting, exercise, lifestyle, sleep, and optimize labs.
- Educate patients about newer strategies for longevity (role of longevity genes and life extension).

Modern Society and Aging

- People don’t want to age
- Our society embraces youth
- Politically incorrect jokes
- Examples


ONE DAY YOU'RE A REAL HOTDOG.
BOWSER
THEN SUDDENLY, YOU BECOME A TIRED OLD WEENIE.


Five
Early Warning Signs
That You're Getting Older:
1. You Repeat Yourself Without Knowing it.
2. You Notice Your Stockings Are Sagging But You're Not Wearing Any.
3. You Can Gauge Wind Direction By Which Way The Skin Under Your Arm is Blowing.
4. You're Still A Hot Chick Only Now it Comes in Flashes.
5. You Repeat Yourself Without Knowing it.


Feeling young is
just a state of mind...
2-620
Brought upon by a pitcher
of margaritas and some cheap wine.
tomato
Cards

Ever notice how a person's mental processes tend to slow down as they get older?

...take your time

...you don't have to answer me right now...

there's no rush...

Happy... Birth... day...


What's your secret for staying so young?
And don't tell me it's diet and exercise. I tried that stuff for almost an hour and it didn't work!
AB

Quick thoughts on Aging

- In Roman times, average age of death was approximately 22.
- In 1800 late 30's
- In 1900 average of death around 48.
- In 1960's 68
- Today is 79.3 years.
- Average age of death increasing the last 165+ years

Quick thoughts on Aging-Continued

- Madam Jeanne Calment of France lived to 122
- What is the maximum potential human life span?
  - Answer- most experts say 115 years!

Theories of Aging

- Wear and tear theory Weissman
- Disposable soma theory
- Anti-oxidant stress and free radical theory
- Neuroendocrine theory-hormone and stem cell decline
- Telomere Theory

Neuroendocrine Theory:

- We age because our hormones and stem cell decline
- Age Management patients with youthful hormones and stem cells may live to the maximum human potential of 115.

Markers that affect Health and Aging

- Insulin levels
- Glycosylated Hemoglobin (HGB-AIC)
- C-Reactive Protein
- Homocysteine Level
- DNA Methylation age-research now
- Measurement of Telomeres

C-Reactive Protein

- Risk factor for illness
- Produced in liver
- Can rise to 1000 fold in acute illness
- Inflammatory cytokines activate
- "CRP worse that LDL" NEJM Nov. 14, 2002
- Diabetes and inflammation is associated
- Higher BMI and Obesity is associated with higher CRP levels
- Cardiorespiratory fitness levels were inversely associated with CRP values

Homocysteine

- Inflammatory amino acid byproduct.
- Can accumulate due to lack of B6, B12, Folate and/or MTHFR mutations-common
- Levels >14 associated with significantly increased risk of cardiovascular disease-stroke or heart disease.
- What is your homocysteine level?
- May be as or more important than cholesterol

Homocysteine Continued

- Common genetic defect of 5-methylethyltetrahydrofolate reductase-may be present in 10 to 20% of population
  - Homocysteine accumulates
  - Highly associated with atherosclerotic disease
    - Stroke
    - Cardiovascular disease
    - Aneurysms
    - hypercoagulation

Homocysteine continued

- Metabolic pathways require co-factors to convert homocysteine to methionine
- B6
- B12
- Folate
- Deficiencies of these cofactors can contribute to elevated homocysteine levels.
- Treatment is methylated or hydroxylated professional B vitamins-methyl folate, methyl b-12 etc.

Caloric Restriction and fasting Decreases Inflammation and causes life extension

- Decreases inflammatory cytokines
- Many studies that caloric restriction and probably fasting prolongs the lifespan in almost all organisms studied from yeast to mammals.
- CR/fasting increases lifespan by 40% in mouse/rat studies.
- Okinawans- long living humans-adequate nutrition with some caloric restriction.

Age Management diet:

- High good, quality fat, moderate protein, fibrous vegetables-broccoli, cauliflower, exotic lettuce, low carb 10-20%-low glycemic fruit-berries, grain free, lower glycemic starches-not daily.
- Paleo/Keto diet essentially.
- Fasting, modified fasting-may be helpful for weight loss, boosting hormones, brain neobiogenesis.

Thoughts on Exercise

- Vital for health, activates sirtuins (longevity genes)
- Adults need one hour per day = 4% of total day!
- Important for weight control
- Perceived barriers:
  - No time
  - No emphasis from M.D.
  - Age
  - Disabilities
  - No interest
  - Cost

Balanced Hormone Optimization

- All hormones restored to a robust 30 year old level and monitored by regular serum levels
- Natural (Bioidentical) Hormones only- identical molecular structure to hormones produced by human male or female. No progestins or horse estrogens.
- We do not use Premarin or PREgnant MARes urINe

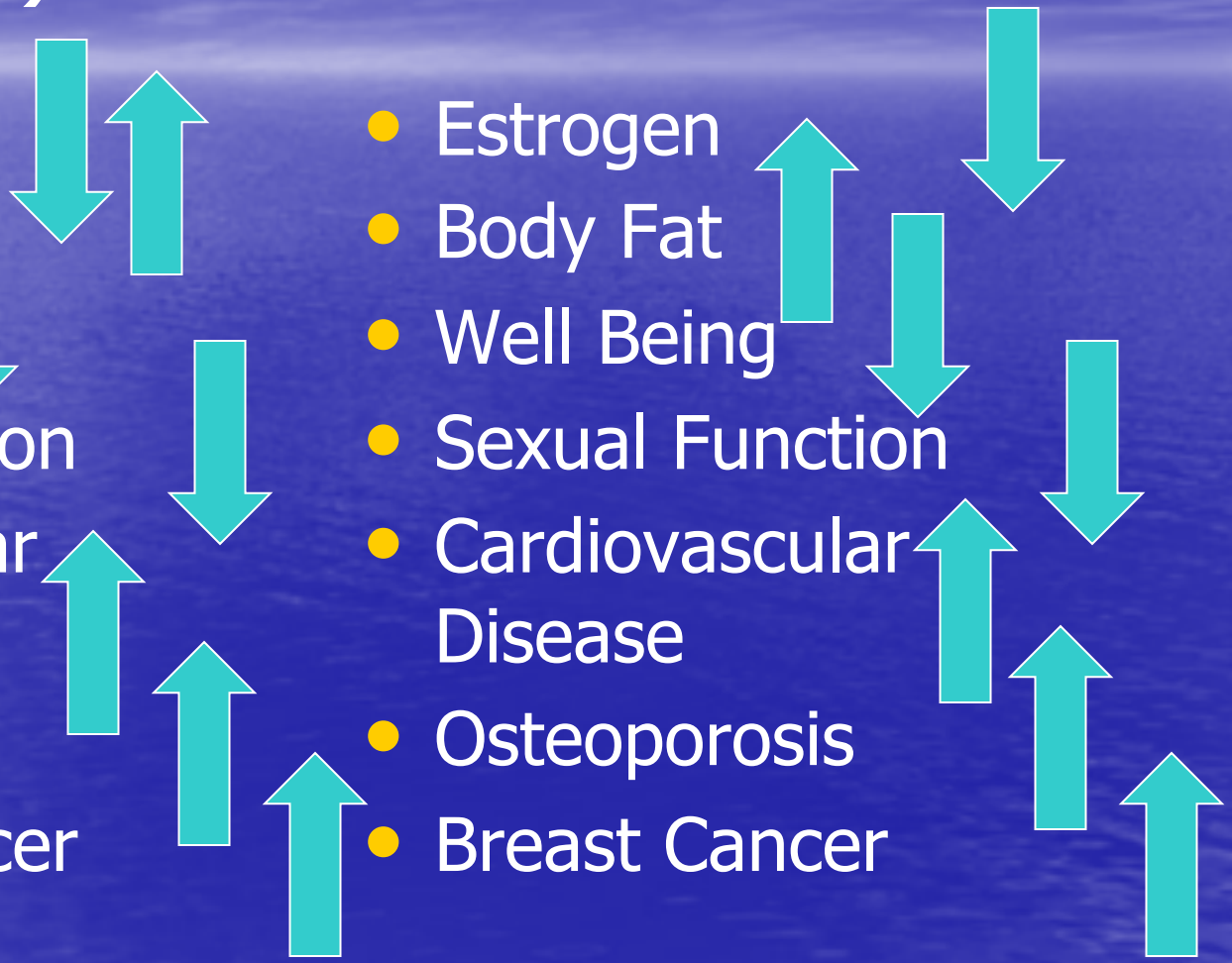
Major Hormones stimulate stem cells and can regenerate organs

- Estrogen, Testosterone, Human growth hormone lower beta amyloid plaque in the brain
- Improve brain function
- Improve body composition
- Less disease, improved quality of life
- Life extension?

Menopause and Andropause (Male Menopause)

- Testosterone
- Body Fat
- Well Being
- Sexual Function
- Cardiovascular Disease
- Osteoporosis
- Prostate Cancer

- Estrogen
- Body Fat
- Well Being
- Sexual Function
- Cardiovascular Disease
- Osteoporosis
- Breast Cancer



Balanced Hormone Optimization At AMI

- Estrogen, Progesterone, Testosterone in women
- Testosterone in men
- Human Growth Hormone
- DHEA
- Pregnenolone
- Melatonin
- Thyroid (T4 and T3), not just T4

Age Management Medicine

- 21st century medicine that is proactive and is advanced preventative medicine.
- Optimal nutrition/supplementation, diet, exercise, bioidentical hormone replacement to youthful levels, repair leaky gut, restore microbiota with probiotics.
- improve body composition, lower inflammatory cytokines, lower inflammation and slow the development of chronic disease AND improve quality of life.

Superlongevity or radical life extension newer strategies

- Activate longevity genes -sirtuins, heat shock proteins
- Potential reversal of epigenetic changes to our DNA. Monitor DNA methylation age in near future.
- Telomere measurement

What does not kill or damage us severely...may cause life extension

- exercise, red wine, mediterranean diet may add 14 years longevity
- caloric restriction in all species studied
- fasting stimulates sirtuins and longevity
- heat-Finnish studies high heat 20 minutes 4-7 times per week = 50% reduction in Cardiovascular disease
- hypothermia-cold plunges, cold shower

Stressors that may increase Longevity

- radiation/Heat-infrared sauna, Japanese used to use x-rays deliberately for longevity purposes
- red light therapy-boosts mitochondria
- regular phlebotomy (blood donation)-blood loss activates longevity?
- low dose alcohol?-many studies show associated longevity with moderate usage

Metabolic Pathways that may be associated with life extension

- Sirtuin longevity pathway-resveratrol, NAD stimulate
- AMPK stimulation-Metformin-life extension, cancer protective effects, stimulates sirtuins-mimics the effects of caloric restriction
- MTOR inhibition-Rapamycin extends longevity in mice, but toxic to humans,

MTOR and Rapamycin continued

- currently felt to be too toxic
- Multiple drug studies ongoing to try to inhibit MTOR by rapalogues that are safer
- Rapamycin is used in organ transplantation but rather severe side effects.

Senolytics to kill Zombie Cells

- Cells that have divided 40-60 times and no longer divide
- Epigenetic changes to DNA inhibit the removal of these
- produce bad cytokines, damage healthy cells
- Quercetin, dasatinib in mice killed the Zombie cells with 36% life extension

Zombie cells continued

- Currently human trials of senolytics initiated 2018 that could have huge potential for human longevity pending safety and side effect profile are acceptable.

My current recommendations

- Metformin-type 2 diabetic drug 500-2000 mg per day typical range
- AMPK activation
- safe multiple studies show anti-cancer effects, life extension, dementia, cardiovascular disease, frailty, depression, makes more NAD
- TAME study-targeting aging with metformin in progress

Current recommendations Continued

- Nicotinamide adenine dinucleotide (NAD)
- declines with aging
- activates sirtuins, DNA damage repair systems
- Provides protons and electrons to the electron transport chain for the production of ATP-the universal cellular energy molecule.

NAD continued

- Nicotinamide riboside (NR)-250-500 mg per day
- Nicotianmide mononucleotide (NMN)
- Combo of both ?

Addition supplements not discussed

Probably helpful-beyond the scope of today

- Resveratrol-100 mg to 1000 mg per day
- Pterostilbene-50-150 mg twice daily
- Astaxanthin-2-12 mg per day
- Curcurmin
- Carnosine 500 mg twice daily
- Alpha Lipoic Acid
- Apigenin 50 mg per day

Additional supplements-not covered but probably helpful

- Sulforaphane-varies
- EGCG-400-500 mg per day, hot organic green tea = 50 mg per cup
- Astragalas -TA-65 100-250 units daily, cycloastrogenol 5-25 mg per day
- Melatonin 3 to 10 mg per day
- Pyridoxamine 50-250 per day

Recommended Reading

- Lifespan by David Sinclair 2019
- The Kaufmann Protocol by Sandra Kaufmann, MD 2016

  -excellent book for prior supplements and adjuvants.

  Thank you!

  markgunderson@renoami.com if you desire a copy of this lecture.

AMP Kinase

- Known as the metabolic master switch
- Helps in production of ATP
- Promotes autophagy, mitochondrial biogenesis
- Declines with aging
- Caloric mimetics that trigger include metformin, resveratrol/pterostilbene, ECGC, quercetin, curcumin

Sirtuins

- Genes and proteins that play a big role in anti-aging.
- 7 genes in mammals
- Regulates longevity, circadian rhythms, disease prevention, metabolism, cell division, telomere length, and can reverse epigenetic changes to our DNA.

Sirtuins continued

- Decline with aging, and essential to aging
- Exercise, caloric restriction/fasting activate sirtuins which can then reverse some epigenetic changes to our DNA, up regulate DNA damage repair systems, help and repair damaged proteins. Yeast given a 3rd sirtuin gene (normally just two) double their lifespan!

Nicotinamide Adenine Dinucleotide (NAD)

- Essential part of energy production of ATP by transporting electrons and protons in the electron transport chain in the mitochondria
- Stimulates sirtuins
- Nicotinamide riboside (NR) and NMN are both used. Combo of both may be best?