Sarah Booth, Ph.D.
Center director, lab director and senior scientist

Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University (HNRCA)

May 23, 2019
A LITTLE BIT OF HISTORY

Food and Agriculture Act of 1977:

Congress hereby finds that there is evidence of a relationship between nutrition and many of the leading causes of death in the U.S.; that improved nutrition is an integral component of preventive health care; that there is a serious need for research on the effects of diet and degenerative diseases and related disorders...one of the largest research centers in the world studying nutrition and physical activity in healthy and active aging and the prevention of age-related disease.

Tufts operates the HNRCA through a cooperative agreement with the USDA

12 Scientific Laboratories
6 Core Units

hnrca.tufts.edu
A LITTLE BIT OF HISTORY

1950: Total 12.3 million Americans 65 or older

NUTRITION RECOMMENDATIONS ARE BASED ON 20TH CENTURY REALITIES

- 65 to 85
- 85 & older

<table>
<thead>
<tr>
<th>Year</th>
<th>65 to 85</th>
<th>85 &amp; older</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950</td>
<td>11.7</td>
<td>11.7</td>
</tr>
<tr>
<td>2015</td>
<td>41.4</td>
<td>65.8</td>
</tr>
<tr>
<td>2050</td>
<td>17.9</td>
<td>83.7</td>
</tr>
</tbody>
</table>

1950: 12.3 million Americans 65 or older
A company is an association or collection of individuals, whether natural persons, legal persons, or a

Smoking and heart disease have decreased.

Obesity and cancer have increased.

Dementia is on the rise.

The number of falls and fractures has skyrocketed.

TIMES HAVE CHANGED
21st century realities in our aging population
Inflammation & immunity
Neuroscience & nutrition
Genomics & epigenetics
Eye health

Cancer prevention
Obesity & diabetes
Musculoskeletal health
Cardiometabolic health

COMPREHENSIVE NUTRITION AND AGING RESEARCH
Bone Mass over the Lifespan in Females

Bone Mass

10  20  30  40  50  60  70  80
Age related changes in the trabecular architecture of vertebrae

Loss of bone mass and horizontal trabeculae

Risk Factors for Osteoporosis

MODIFIABLE

Poor diet –
- low vitamin D & Ca,
- acid-base imbalance
Sedentary
Smoking
Excess alcohol
Early loss of estrogen
Thinness

NOT MODIFIABLE

Age
Heredity
Medications- steroids, heparin
Effect of and **Vitamin D (700 IU/d)** and Calcium (500 mg/d) on Non-vertebral Fracture Rates in Healthy Men and Women

Impact of Discontinuing Vitamin D and Calcium on Femoral Neck BMD in Men

Achieved 25(OH)D serum concentration in treatment group (nmol/l)

RR (95% CI)

200 IU
400 IU
600 IU
800 IU
800 IU
800 IU
800 IU
700 IU

Effect of High Dose Vitamin D on Falls and Fractures in 2,256 Women age 70+ 
(500,000 IU orally once per year)

Falls

HR, 1.16 (95% CI, 1.05-1.28)  
P = .003

Fractures

HR, 1.26 (95% CI, 0.99-1.59)  
P = .06

* Sanders KM. JAMA 2010;303:1815-1822.
Vitamin D - Conclusions

Vitamin D supplementation, as needed, to reach a daily intake of 600-800 IU/d is important for bone health.

Vitamin D is most effective when taken together with calcium.

High intermittent doses of vitamin D *increase* risk of falls and fractures in older adults.

There is no evidence that recommended doses (600 to 800 IU/d) have any safety concerns.
Hypothesis: Acid-producing diets contribute to bone and muscle loss

Americans consume 2x the recommended amounts of grains and half the recommended amounts of fruits and vegetables.

American diets therefore are acidogenic or acid producing (because the sulfur in cereal grains and protein is metabolized to sulfuric acid and fruits and vegetables are metabolized to bicarbonate).

Acid-base balance is assessed indirectly by measuring the excretion of acid or base in the urine (i.e., ‘net acid excretion’). For example, the presence of acid in the urine reflects inadequate intake of fruits and vegetable relative to the intake of grains and protein).
Of 171 Healthy Older Men and Women Recruited for a Recent Study, 96% were excreting acid in the urine, indicating that they were consuming acid-producing diets.
Can reversing acid producing diets improve muscle and bone health?

We conducted a clinical trial in 171 healthy older men and women.

They were treated with potassium bicarbonate or no bicarbonate daily for 3 months.

Muscle assessments: nitrogen excretion (an index of muscle loss) and leg power

Bone assessments: calcium excretion and bone resorption.
RCT: Effect of Bicarbonate on Nitrogen Excretion
(171 men and women age 50+, 67.5 mmol/kg dose)

Group difference in women $P = 0.004$

Bicarbonate improved double leg press peak power output in women but not in men.
Bicarbonate (67.5 mmol/d for 3 mo) reduces calcium excretion, urinary NTX, and net acid excretion

P < 0.001 for each

Conclusions

Acid-producing diets contribute to muscle and bone loss.

This loss can be reduced with alkali (potassium bicarbonate) pills.

Up next? Can muscle and bone be protected by diet modification that restores acid-base balance?
Examples of acid producing (+), neutral (0), and alkali producing (-) foods

<table>
<thead>
<tr>
<th>Acid Producing (+)</th>
<th>Neutral (0)</th>
<th>Alkali Producing (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parmesan cheese</td>
<td>34.0</td>
<td>Wine</td>
</tr>
<tr>
<td>Chicken</td>
<td>8.7</td>
<td>Oranges</td>
</tr>
<tr>
<td>Lean beef</td>
<td>7.8</td>
<td>Pears</td>
</tr>
<tr>
<td>Fish</td>
<td>7.0</td>
<td>Raisins</td>
</tr>
<tr>
<td>Oatmeal</td>
<td>10.7</td>
<td>Carrots</td>
</tr>
<tr>
<td>Brown rice</td>
<td>12.5</td>
<td>Tomatoes</td>
</tr>
<tr>
<td>Bread</td>
<td>4.0</td>
<td>Celery</td>
</tr>
<tr>
<td>Milk, yogurt</td>
<td>1.0</td>
<td>Spinach</td>
</tr>
<tr>
<td>Oils</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Roger Fielding, Ph.D
Associate center director, lab director and senior scientist

Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University (HNRCA)

May 23, 2019
Mobility disability in the US in 2010

About 23.9 million people living in the community had difficulty walking a quarter of a mile.

13.1 million who could not perform this activity.

Among those aged 65 and older living in the community, 39.4% had difficulty with ambulatory activities.

11.2 million had severe difficulty.

US Census Bureau, Current Population Reports, MW Brault, July 2012, P70-131
Skeletal Muscle Matters!

45-50% of body mass

Fundamental role in locomotion, O$_2$ consumption, whole-body energy metabolism, and substrate turnover and storage

Secretory orga (“myokines”)

Robust skeletal muscle is a central factor in whole-body health and essential for maintaining energy homeostasis

Mobility across species (highly conserved motor proteins)

Aging and physical performance

**Drosophila**

**A**

![Graph showing survival over age](image)

- Young (3 days)
- Median (49 days)
- Old (56 days)

**B**

![Bar graph showing flight index over age](image)

- Flight Index
- Unable to fly

**C**

![Bar graph showing WBF (Hz) over age](image)

- WBF (Hz)
- No wing beat

**Rats**

**A**

![Bar graph showing mean survival time by quartiles](image)

- Quartiles of Summary Performance Score
- p for trend = .033
- n = 12 in each quartile

**B**

![Graph showing survival probability over months](image)

- Survival Probability, %
- p = .017

*Miller et al. Biophys J 2008;95:2391*

*Carter et al. J Gerontol 2002; 57:B193*
Median Life Expectancy According to Age and Gait Speed

Men

Women

# Economic costs of physical inactivity

## Economic Burden
Cost in billion international $ (BLN)

<table>
<thead>
<tr>
<th>Country</th>
<th>Cost (BLN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>27.79</td>
</tr>
<tr>
<td>Japan</td>
<td>5.26</td>
</tr>
<tr>
<td>China</td>
<td>4.86</td>
</tr>
<tr>
<td>Germany</td>
<td>2.72</td>
</tr>
<tr>
<td>UK</td>
<td>2.41</td>
</tr>
</tbody>
</table>

*Lancet, 2016, 388: 1311-24*
Sarcopenia: Age-associated loss in muscle mass and function

Components:
- Muscle mass
- Muscle strength
- Physical performance
Interventions for sarcopenia:

**Lifestyle Interventions**
- Physical activity/Exercise (Resistance training/multi-modal training)
- Nutrition/dietary intake (Protein, Vitamin D, Omega-3 fatty acids)

**Pharmacologic Interventions**
- Muscle growth
- Neuromuscular/contractile properties
- Energy transduction (eg: mitochondrial biogenesis)
- Medicines currently approved for other indications

**Combination therapies**
Progressive Resistance Exercise Training
(1 yr 2 X per wk)
Lean Mass change after 1 yr. of resistance exercise training

Muscle mass (kg)

Control group
Exercise group

* p=0.03
• Design: Pilot study (LIFE-P) followed by a Phase 3 RCT (LIFE-M)

• LIFE-P N = 425 (4 clinical centers)

• LIFE-M N = 1600 (8 clinical centers)

• Mean FU: LIFE-P=1 year; LIFE-M=2.7 years (min 1.9 - max 3.9 years)

• Intervention: aerobic + resistance exercise vs. health education

*Fielding et al. J. Gerontol. 2011
Physical activity intervention center-based in a group setting

- Aerobic (walking)
- Strength (lower extremities)
- Balance
- Flexibility stretching
- Behavioral counseling (group and telephone)
HR=0.82, 95%CI=0.69-0.98
p=0.03

Pahor et al JAMA 2014
Nutrition/Exercise interactions: VIVE2 Study Intervention

Exercise Intervention
(3x/week for 6 months)

- Walking
- Strength training (chair and ankle weight)
- Flexibility
- Balance

Nutritional supplement
(daily)

- Nutritional supplement- Whey protein (20g), vitamin D (800 IU), calcium, vitamins + minerals (150 kcal)
- Placebo- non-nutritive sweeteners (30 kcal)

Kirn et al Cont Clin Trials 2015
Effects of Physical activity plus nutritional supplement on thigh muscle quality
Effects of Physical activity plus nutritional supplement on intermuscular fat

Englund et al J Gerontol 2017
Exercise/physical activity remains the only treatment for improving physical function and preventing disability.
Physical Activity Guidelines for Adults:

Some physical activity is better than none.

For substantial benefits, adults should do at least 150 minutes a week of moderate-intensity, or 75 minutes a week of vigorous-intensity aerobic physical activity.

For more extensive health benefits, adults should increase their aerobic physical activity.

Adults should also do muscle-strengthening activities that are moderate or high intensity and involve all major muscle groups on 2 or more days a week.
When older adults cannot do 150 minutes of moderate-intensity aerobic activity a week because of chronic conditions, they should be as physically active as their abilities and conditions allow.

Older adults should do exercises that maintain or improve balance if they are at risk of falling.

Older adults should determine their level of effort for physical activity relative to their level of fitness.

Older adults with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely.