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The Impact of Nutrition on Aspects of Healthy Aging

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Successful Aging

- Psychological: emotional vitality
- Sociological: engaging with life, spirituality
- Physiological: impairment, disease
- Genetic

Diet?
Successful Aging

- Psychological: emotional vitality
- Sociological: engaging with life, spirituality
- Physiological: impairment, disease
- Genetic

Diet!
Age-related Declines in Physiological Function

- Nerve conducting velocity
- Maximum heart rate
- Kidney blood flow
- Maximum breathing capacity
- Maximum work rate (oxygen uptake)
- Female fertility
Functional Interconnections Between Hallmarks of Aging

López-Otin et al. *Cell* 2013
Telomere Attrition

As the cell divide overtime (healthy cell)...

...telomeres shorten until cell division stops (senescence).
Curcumin, Flavanols, Genistein, Sulforaphane downregulate telomerase reverse transcriptase
Multivitamin Use is Positively Associated with Telomere Length in Women

Sister Study

Cohort XS
- n, 586
- age, 35-74

Xu et al. Am J Clin Nutr 2009
DNA Damage Response and Aging

Exogenous sources
Radiations, chemicals...

Endogenous sources
ROS, replication errors, hydrolysis...

Accumulation of DNA damage

DNA repair mechanisms
Decline of efficiency and accuracy of DNA repair

Cancer
Mutagenic lesions

Defects of cellular functions
Cytotoxic or cytostatic lesions

Cell death and senescence

AGING

Nicolai et al. Aging 2015
β-Carotene, Lutein, and/or Lycopene Protect Against DNA Damage

RCT
- n, 37 women
- age, 50-70 y
- duration, 56 d
- dose, 12 mg/d


<table>
<thead>
<tr>
<th>Group</th>
<th>Day 1</th>
<th>Day 15</th>
<th>Day 29</th>
<th>Day 43</th>
<th>Day 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endogenous DNA damage (%)²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 6)</td>
<td>8.7 ± 0.8</td>
<td>9.0 ± 1.0</td>
<td>10.6 ± 1.3</td>
<td>9.2 ± 1.7</td>
<td>9.9 ± 1.5</td>
</tr>
<tr>
<td>Mixed carotenoids (n = 8)</td>
<td>10.9 ± 0.6</td>
<td>8.6 ± 0.6³</td>
<td>7.9 ± 0.7³</td>
<td>7.1 ± 0.5³</td>
<td>7.0 ± 0.4³</td>
</tr>
<tr>
<td>Lutein (n = 8)</td>
<td>10.6 ± 0.5</td>
<td>9.4 ± 0.7</td>
<td>9.5 ± 0.5</td>
<td>7.7 ± 0.5³</td>
<td>7.1 ± 0.6³</td>
</tr>
<tr>
<td>β-Carotene (n = 7)</td>
<td>12.4 ± 1.0³</td>
<td>9.7 ± 0.9³</td>
<td>8.6 ± 1.1³</td>
<td>9.4 ± 0.9³</td>
<td>8.0 ± 0.7³</td>
</tr>
<tr>
<td>Lycopene (n = 8)</td>
<td>11.9 ± 0.9</td>
<td>10.0 ± 1.2</td>
<td>9.0 ± 0.9³</td>
<td>7.5 ± 0.7³</td>
<td>6.8 ± 0.6³</td>
</tr>
<tr>
<td>Hydrogen peroxide–induced DNA damage (%)⁶</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 6)</td>
<td>42.1 ± 2.2</td>
<td>44.6 ± 2.4</td>
<td>39.7 ± 1.1</td>
<td>43.0 ± 2.9</td>
<td>40.6 ± 3.1</td>
</tr>
<tr>
<td>Mixed carotenoids (n = 8)</td>
<td>44.2 ± 2.5</td>
<td>43.2 ± 3.3</td>
<td>42.6 ± 2.9</td>
<td>37.1 ± 4.0</td>
<td>36.4 ± 2.2</td>
</tr>
<tr>
<td>Lutein (n = 8)</td>
<td>42.8 ± 2.4</td>
<td>43.5 ± 2.2</td>
<td>43.1 ± 2.0</td>
<td>41.5 ± 3.3</td>
<td>39.8 ± 3.0</td>
</tr>
<tr>
<td>β-Carotene (n = 7)</td>
<td>48.2 ± 2.3</td>
<td>44.5 ± 3.4</td>
<td>41.1 ± 2.4</td>
<td>44.2 ± 2.1</td>
<td>38.0 ± 1.8</td>
</tr>
<tr>
<td>Lycopene (n = 8)</td>
<td>50.5 ± 3.2</td>
<td>49.2 ± 3.6</td>
<td>51.1 ± 1.2</td>
<td>50.0 ± 2.3</td>
<td>42.5 ± 2.3</td>
</tr>
</tbody>
</table>
DNA Damage: Genetics vs. Epigenetics
HATs Relax Chromatin ➔ Gene Activation
HDACs Close Chromatin ➔ Gene Repression

Meeran et al. *Clin Epigenetics* 2010
# Epigenetic Targets of Phytochemicals

<table>
<thead>
<tr>
<th>Dietary Bioactive</th>
<th>Epigenetic Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apigenin</td>
<td>↓DNMT</td>
</tr>
<tr>
<td>Allyl mecaptan</td>
<td>↓HDAC</td>
</tr>
<tr>
<td>Curcumin</td>
<td>↓DNMT, HDAC, HAT</td>
</tr>
<tr>
<td>EGCG</td>
<td>↓DNMT, HAT</td>
</tr>
<tr>
<td>Genistein</td>
<td>↓DNMT, HDAC ↑HAT</td>
</tr>
<tr>
<td>Resveratrol</td>
<td>↓DNMT ↑SIRT1</td>
</tr>
<tr>
<td>Silymarin</td>
<td>↑SIRT1</td>
</tr>
<tr>
<td>Sulforaphane</td>
<td>↓DNMT, HDAC</td>
</tr>
</tbody>
</table>

Meeran et al. *Clin Epigenetics* 2010
Mitochondrial Dysfunction as a Target for Aging

López-Otin et al. *Cell* 2013
Dynamic Network Links Cellular Pathways of Inflammation and Mitochondrial Function to Food and Nutrients

Anti-inflammatory Actions of Vitamin E

RCT
- n, 75
- age, 57 y
- F/U, 3 mo
- dose, 1200 IU/d

Devaraj et al. *Circulation* 2000
Supoptimal Dietary Patterns are a Leading Cause of Poor Health

Mozaffarian *Circulation* 2016
Evidence-based Dietary Priorities for Cardiometabolic Health

- Benefit
  - Fruits, Nuts, Fish
  - Vegetables, Vegetable Oils
  - Whole Grains, Beans, Yogurt
  - Cheese
  - Eggs, Poultry, Milk
  - Butter
- Harm
  - Unprocessed Red Meats
  - Refined Grains, Starches, Sugars
  - Processed Meats, High Sodium Foods
  - Industrial Trans Fat

Mozaffarian *Circulation* 2016
Multivitamins Reduce the Risk of Total Cancer

*Physicians’ Health Study II*

**Primary Prevention**
- HR: 8% ↓
- HR (≥70 y): 18% ↓

**Secondary Prevention**
- HR: 27% ↓

**RCT**
- n, 14,641 men
- age, ≥50 y

Gaziano et al. *JAMA* 2012
Antioxidants Slow Progression to Age-Related Macular Degeneration

Age-Related Eye Disease Study

Flavonoid Intake at Midlife Promotes Healthy Aging in Women
Nurses’ Health Study

Prospective Cohort
• n, 13,818
• age, 74 y
• F/U, 15 y

Healthy Aging Criteria
• Survive to ≥70 y
• No major chronic diseases
• No major physical impairments in cognitive, physical function or mental health

**Flavonoid Intake at Midlife Promotes Healthy Aging in Women**  
*Nurses’ Health Study*

1517 of 13,818 women (11%) met criteria for healthy aging

<table>
<thead>
<tr>
<th>Flavonoid</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavonols</td>
<td>18%</td>
</tr>
<tr>
<td>Flavones</td>
<td>32%</td>
</tr>
<tr>
<td>Flavanones</td>
<td>28%</td>
</tr>
<tr>
<td>Anthocyanins</td>
<td>25%</td>
</tr>
<tr>
<td>Total Flavonoids</td>
<td>47%</td>
</tr>
</tbody>
</table>

Anthocyanins Reduce the Risk of Incident Hypertension and Myocardial Infarction

*Nurses Health Study II*

<table>
<thead>
<tr>
<th>Quintile</th>
<th>iHT</th>
<th>MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>6%↓</td>
<td>20%↓</td>
</tr>
<tr>
<td>3</td>
<td>7%↓</td>
<td>29%↓</td>
</tr>
<tr>
<td>4</td>
<td>9%↓</td>
<td>15%↓</td>
</tr>
<tr>
<td>5</td>
<td>13%↓</td>
<td>32%↓</td>
</tr>
<tr>
<td><em>P</em></td>
<td>0.0001</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Healthy Aging as Outcome Criteria

**SU.VI.MAX 2**

**RCT**
- n, 3996
- age, 65.3 ± 4.5 y
- intervention, 8 y
- F/U, 15 y

**SUPPLEMENT**
- Vitamin C, 120 mg
- Vitamin E, 30 mg
- β-carotene, 6 mg
- Selenium 100 µg
- Zinc, 20 mg

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<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
<th>Corresponding Rowe and Kahn Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good physical functioning</td>
<td>SPPB ≥11 of 12</td>
<td>Maintenance of high physical and cognitive function</td>
</tr>
<tr>
<td>Good cognitive functioning</td>
<td>MMSE ≥27, RI-48 ≥19 of 48, and DK-TMT ≥5.5</td>
<td>Maintenance of high physical and cognitive function</td>
</tr>
<tr>
<td>No limitations in IADL</td>
<td>&lt;1 limitation</td>
<td>Avoiding disease and disability</td>
</tr>
<tr>
<td>No depressive symptoms</td>
<td>CES-D &lt;16 of 60</td>
<td></td>
</tr>
<tr>
<td>No health-related limitations in social life</td>
<td>SF-36 responses: 1–2 for item 6 and 3–5 for item 10</td>
<td>Sustained engagement in social and productive activities</td>
</tr>
<tr>
<td>Good overall self-perceived health</td>
<td>SF-36 responses: 1–3 for item 1</td>
<td></td>
</tr>
<tr>
<td>No function-limiting pain</td>
<td>SF-36 responses: 1–3 for item 7 and 1–2 for item 8</td>
<td>Avoiding disease and disability</td>
</tr>
<tr>
<td>No incident major chronic disease</td>
<td>No incident diabetes, cancer, or cardiovascular disease during follow-up</td>
<td>Avoiding disease and disability</td>
</tr>
</tbody>
</table>

Antioxidant Supplementation as a Predictor of Healthy Aging

<table>
<thead>
<tr>
<th>Stratification Variable</th>
<th>Total n</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>3996</td>
<td>7%</td>
</tr>
<tr>
<td>Men</td>
<td>2027</td>
<td>16%</td>
</tr>
<tr>
<td>Vitamin C status, &lt;42 µmol/L</td>
<td>727</td>
<td>28%</td>
</tr>
<tr>
<td>Zinc status, &lt;11.9 µmol/L</td>
<td>953</td>
<td>26%</td>
</tr>
<tr>
<td>F&amp;V (&lt;400 g/d)</td>
<td>1757</td>
<td>17%</td>
</tr>
</tbody>
</table>
Lutein is Concentrated in Brain and Correlated with Cognitive Performance in Elderly

The Georgia Centenarian Study

Johnson et al. *J Aging Res* 2014
Lutein/Zeaxanthin Supplementation Reduces Psychological Stress and Serum Cortisol

RCT
• n, 59
• age, 21.5 y
• BMI, <27.0

Stringham et al. Nutr Neurosci 2017
Depression is one of the most prevalent and disabling disorders in the EU. MooDFOOD is one of the largest consortia investigating depression, and the first to address the role of nutrition in its prevention.

**ABOUT:**

**RCT**
- n, 1000
- age, 18-75 y
- BMI, 25-40
- duration, 12 mo

**Supplement**
- EPA + DHA, 1412 mg
- calcium, 100 mg
- selenium 30 µg
- folic acid, 400 µg
- vitamin D3, 20 µg

Roca et al. *BMC Psychiatry* 2016
The Secret of Healthy Aging
The Role of Essential Nutrients in the Continuum of Health

Sick

Not Sick

Well
WHO - Active Ageing: A Policy Framework

- Prevent and reduce the burden of excess disabilities, chronic disease and premature mortality
- Reduce risk factors associated with major diseases and increase factors that protect health throughout the life course
- Develop a continuum of affordable, accessible, high-quality and age-friendly health and social services that address the needs and rights of people as they age
- Provide training and education to caregivers
