Symposium 5 – The Nutrition Society Symposium
Muscle Wasting with Age – A New Challenge in Nutritional Care
Part 1 – The Underlying Factors
Ageing and Taste

Dr Lisa Methven

Food and Sensory Scientist
Introduction—Background

- Malnutrition: *state of being poorly nourished*
- Prevalence of undernutrition in UK
  - 60% of older people are at risk of becoming malnourished in hospital (Age Concern, 2006)
  - In 2007, ca. 50,000 people died in English hospitals with malnutrition; for 239 patients, malnutrition was the direct cause of death
- Effects of malnutrition:
  - Economic and social costs
  - Predisposes to disease
  - Longer period of illness
  - Increased mortality rate
  - Liable to increased complications during surgery
  - More likely to be discharged into care
Background - Causes

• Why is malnutrition common among older people?

  - Physiological
  - Psychological
  - Socio-economic

  Diminished sensory ability: Taste and smell deterioration caused by ageing or due to medication and illness

• Taste as a factor in the management of nutrition
  - (Scott and Verhagen 2000)
## Literature on Taste Detection & Age

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Bales et al., 1986           | YP (n=30) (18-30, av. 24)                          | Salt detection ↑ 3.8x  
Sweet (sucrose) detection ↑ 1.4x                                         |
|                              | OP (n=32) (60+, av. 73)                            |                                                                          |
| Drewowski et al., 1996       | YP (n=24) (20-30)                                  | Salt detection YP=OP                                                     |
|                              | OP (n=24) (60-75)                                  |                                                                          |
| Fukunaga et al., 2005        | YP (n=30) (18-29, av. 24)                          | Sweet (sucrose), Salt and Sour (tartaric) all ↑ significantly  
Bitter (quinine) variable                                           |
|                              | OP (n=30) (65-85, av. 75)                          |                                                                          |
| Kaneda et al., 2000          | YP (n=20) (20-40, av. 29)                          | Detection thresholds ↑, except sweet.                                     |
|                              | OP (n=20) (59-75, av. 67)                          |                                                                          |
| Matsuda and Doty, 1995       | YP (n=12) (20-29, av. 24)                          | Salt detection ↑                                                         |
|                              | OP (n=12) (70-79, av. 75)                          |                                                                          |
| Mavi and Ceyhan, 1999        | YP (n=30) (17-25, av. 20)                          | Bitter detection ↑                                                       |
|                              | OP (n=24) (60-80, av. 69)                          |                                                                          |
Sweetness (aspartame) and Bitter (quinine) detection YP=OP.  
Above threshold: Decreased intensity for salty & sweet, but not sour, bitter or umami. |
|                              | OP (n=21) (60-75, av. 65)                          |                                                                          |
| Ng et al., 2004              | YP (n=26) (21-34)                                  | Taste thresholds ↑> 70 years                                              |
|                              | Middle-Aged (n=13) (36-61)                         |                                                                          |
|                              | OP (n=24) (69-94)                                  |                                                                          |
| Receputo et al., 1996        | Centenarians (n=20) (av. 103)                      | Taste was severely reduced in centenarians cf OP and YP                  |
|                              | OP (n=20) (av. 71)                                 |                                                                          |
|                              | YP (n=20) (av. 28)                                 |                                                                          |
| Wayler et al., 1990          | YP (n=30) (55-65)                                  | Suprathreshold: OP needed larger change in NaCl concentration to perceive |
|                              | OP (n=37) (65-78)                                  |                                                                          |
Taste Thresholds: Why They May Increase with Age

- **Morphological changes** - decrease in receptor numbers
- **Functional changes** of gustatory cells
- **Neural noise hypothesis** – the signal to noise ratio in the brain is lowered by decrease in signal intensity and increase in spontaneous firing from the taste receptor cells.
- **Stimulus persistence hypothesis** – the signal from the taste cells continues to be sent to the brain even when stimulus falls below threshold.
- **Perceptual noise hypothesis** - Repetitive neural firing from the taste cells makes brain unable to ignore irrelevant signals.
- **Disinhibition hypothesis** – cognitive inaccuracies make individual unable to retrieve information from memory and connect with current signals from taste cells.

Significant increase in salt and MSG threshold for the patients.
Taste Thresholds: Our Evidence

• Taste Threshold data: collected from three groups:
  – Younger healthy adults
  – Older healthy adults
  – Older hospital patients

• Present participant with series of triads; identify “odd one out” (3AFC)

• Sweet, (sucrose), Salty (NaCl), Umami (glutamate), Bitter (quinine)

• Blood samples: Zinc (Zn) and Selenium (Se) status (older participants only)
Taste Threshold Variability

Salt Taste Detection Thresholds

Umami (glutamate) Detection Thresholds

Bitter (quinine) Detection Thresholds

Older Volunteers (%)
Older Patients (%)
## Taste Detection Thresholds

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean Age(range)</th>
<th>Sweet (sucrose)</th>
<th>Salt (NaCl)</th>
<th>Umami</th>
<th>Bitter (quinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital patients</td>
<td>(50) (42) (51) (28)</td>
<td>84 (65-98)</td>
<td>16 mM (0.5%)</td>
<td>18 mM (0.11%)</td>
<td>3.8 mM (0.07%)</td>
<td>0.03 mM (0.002%)</td>
</tr>
<tr>
<td>Healthy older volunteers</td>
<td>38 (35)</td>
<td>71 (62 – 87)</td>
<td>6 mM (0.03%)</td>
<td>1.8 mM (0.03%)</td>
<td>0.006 mM (0.0005%)</td>
<td></td>
</tr>
<tr>
<td>Healthy younger volunteers</td>
<td>35</td>
<td>(25-35)</td>
<td>2.5 mM (0.01%)</td>
<td>0.5 mM (0.01%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significant increase in Salt, Umami & Bitter threshold between healthy older volunteers and older patients (p<0.001 to p<0.05)
Zinc & Selenium Status Variability

**Selenium Status**

- Frequency (%)
- Selenium (µmol/L)
- Selenium Status
- Older Patients
- Healthy Older Volunteers

**Zinc Status**

- Frequency (%)
- Zinc (µmol/L)
- Zinc Status
- Patients
- Healthy Volunteers
# Zinc & Selenium Status

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean Age (range)</th>
<th>Zn (µmol/L)</th>
<th>% below reference</th>
<th>Se (µmol/L)</th>
<th>% below reference</th>
<th>HADS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital patients</td>
<td>34</td>
<td>84 (71 – 93)</td>
<td>11 ± 6.4</td>
<td>19%</td>
<td>0.8 ± 0.39</td>
<td>56%</td>
<td>13 ± 8</td>
</tr>
<tr>
<td>Healthy older volunteers</td>
<td>38</td>
<td>71 (62 – 87)</td>
<td>13 ± 1.4</td>
<td>0%</td>
<td>1.2 ± 0.21</td>
<td>3%</td>
<td>7 ± 4</td>
</tr>
<tr>
<td>Reference range</td>
<td></td>
<td>8-17</td>
<td></td>
<td></td>
<td>0.8-1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>significance</td>
<td></td>
<td>&lt; 0.0001</td>
<td></td>
<td></td>
<td>&lt; 0.0001</td>
<td></td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Mean serum Zn and Se levels significantly lower for patients.

Anxiety & depression scores (not surprisingly) higher for patients
Zinc & Selenium: a reason to supplement?

- Zinc deficiency reduces taste acuity
  - Zn required for taste cell growth

- Selenium required by thyroid hormones & effects neurotransmitter activity
  - May affect mood; thereby affecting food consumption directly; or may increase taste thresholds.
Zinc & Selenium: Previous studies

**Zinc**

**Zenith study**  
(Stewart-Knox 2005)  
\( n = 199 \) in Zn supp. Study  
Healthy older volunteers  
Salt taste acuity improved  
Mean serum Zn pre-intervention 13\( \mu \)mol/L  

Maybe more effective with patients?  
(our patient mean 11\( \mu \)mol/L; but with 73% lower)

**Selenium**

**Patient study**  
(Gosney 2008)  
\( n = 50 \) in Se supp. study  
Improved mood, decreased anxiety  
Mean serum Se pre-intervention 1.0 \( \mu \)mol/L

**Healthy Older Volunteers**  
(Rayman, 2005)  
\( n = 501 \) in Se supp. study  
No affect on mood  
Improved mood, decreased anxiety  
Mean serum Se pre-intervention 1.2 \( \mu \)mol/L

Lisa Methven, Food & Nutritional Sciences, UoR
Taste Enhancement of Food for Older Hospital Patients
Background- Previous studies

Enhancement of umami taste of food for older people in order to increase consumption

- **Schiffman et al.**: Flavour and/or monosodium glutamate (MSG) led to increased food consumption among older people, increased salivary flow, improved immunity and muscle strength.
- **Bellisle et al. (1998)**: older people preferred food with MSG.
- **Toyama et al. (2008)**: consumption of food with MSG improved routine function and quality of life of older patients.
- **Essed et al. (2009)**: no effect on intake and liking of soup enhanced with MSG.
- **Essed et al. (2007)**: no effect of 16 week flavour and or MSG addition to animal protein on dietary intake and nutritional status of nursing home elderly.
Our approach...

**AIM**

- Improve the palatability of savoury foods for **older hospital patients** in order to stimulate appetite and increase consumption.

**Hypothesis**

- Taste enhancement will increase liking and consumption.
- Taste sensitivity affects their liking and consumption.

**Approach**

- Enhancement of savoury characteristics using **naturally occurring tastants** in hospital food to levels preferred by **older people**
Our approach...

Use of **natural ingredients** rich in **umami** taste compounds

- Maximum levels of “UMAMI” ingredients in a meat dish
- Keep Sodium levels constant
The Umami Taste

- Characteristic taste of Glutamate (MSG) and 5’-nucleotides
- **Multiple Receptors** (Chaudhari, 2009, Am J Clin Nutr, 90, 1S-5S)
- Specific L-glutamate receptors on the tongue, and in stomach
  - mGluR1
  - mGluR4
- Less specific heterodimer T1R1 + T1R3
  - responds to amino acids AND ribonucleotides
- Synergy between the umami amino acids & ribonucleotides
- **Enhancement of savoury volatile flavours**: greater activation shown in cortex taste-olfactory convergence regions of the brain by fMRI (McCabe & Rolls, 2007, E J Neuroscience, 25, 1855-1864)
Umami and Older People

• Dry mouth due to diminished salivation
  – Umami stimulation increases salivary flow (Hodson and Linden, 2006; Schiffman et al.)

• Reduced appetite due to diminished sensory ability
  – Umami sensitivity strongest correlation with human appetite (Shi et al, 2004)
  – Preference for umami is affected by nutritional status (Murphy, 1987)

• Gastric dysfunction
  – Stimulating gastric function through gastric L-glutamate receptors (Toyoma et al, 2008)
  – Chronic atrophic gastritis
    • MSG supplementation of meals was reported to increase basal and maximal acid output to normal amounts and improved appetite (Kochet et al)
  – Delayed gastric emptying
    • MSG in combination with protein rich foods increased gastric emptying rate (Zai et al, 2009)
Umami Amino Acids & Ribonucleotides

- Glutamic acid
- Aspartic acid
- Inosine monophosphate
- Guanosine monophosphate
- Adenosine monophosphate
Methodology

Recipe development
chemical analysis

Sensory profiling
Trained sensory panel
(n=10, mean age 46)

Consumer study 1
Younger (n=31, age 21-32, mean 25)
Older (n=32, age 62-83, mean 73)

Consumer study 2
Older
(n=35, age 62-87, mean 71)

Hospital study
Older hospital patients
(n=31, age 65-92, mean 84)
Optimisation of Recipe

NHS Basic minced meat recipe
Minced meat (42%)
+ Sunflower oil (1%)
+ Onion puree (8.6%)
+ Garlic puree (0.7%)
+ Cornflour (1.7%)
+ Water (beef stock) (43%)
+ Tomato puree (30%TS) (2.8%)
+ Salt (0.2)

Instructions
1. Heat oil
2. Brown beef
3. Cook onion
4. Add garlic tomato puree
5. Add salt
6. Add beef stock and simmer
7. Add cornflour

✓ Maximum possible levels of ingredients
✓ Sodium levels kept constant for all recipes (0.2%)

Additional Ingredients:
✓ MSG
✓ Yeast extracts (maxarome, gistex)
✓ Mycoscent (mycoprotein)
✓ Soy sauce (Kikkoman Low Salt) (SS)
✓ Tomato puree
✓ Honzokuri miso paste (Low Salt)
✓ Shiitake (70°C extract)
✓ Concentrated Tomato Extract
Hospital study: Methods

- Which samples? **Control vs Enhanced cottage pies**
  - Enhanced pie: Soy Sauce and Concentrated Tomato Extract (SS+CTE)
  - Enhanced gravy: soy sauce (SS)
- Where? **Elderly Care Wards in one NHS Trust Fund**
- Volunteers? **31 older (age>65) patients** (11 Male, 20 Female)
- Protocol
  - Consent
  - Screening
  - Liking and preference test on **minced meat**
  - Measurement of consumption of the two **cottage pies** during lunch time
## Hospital study: Results

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Enhanced</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liking minced meat</td>
<td>6.1</td>
<td>6.7</td>
<td>p=0.045</td>
</tr>
<tr>
<td>(9-point)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preference minced meat</td>
<td>7</td>
<td>24</td>
<td>p=0.02</td>
</tr>
<tr>
<td>(number of people)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumption (g)</td>
<td>117.5</td>
<td>137.1</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

- There was a trend for consumption to be affected by liking scores (p=0.125)
- There was a trend for total consumption to be higher where depression scores (HADS) were lower (p=0.06)
Challenges/Limitations

- Consenting & bias to the “least frail”
- Two plates confusing / difficult to handle / overwhelming
- Lunch time too early, volunteers were not hungry
- Some people stated that preferred one sample but decided to eat more of the other one ?!
- Older people score liking high to please the researcher
- Repeat exposure may affect consumption of enhanced meals – not taken into account here
Conclusions

- Thresholds increase with age & illness/medication. Salt thresholds increased more than glutamate.

→ Logical approach to enhance umami taste of food for older people

- Natural ingredients successfully used to enhance the taste of food
- Majority of patients preferred enhanced minced meat
- No significant differences in consumption of the different samples
- Consumption can be affected by mood
- More factors need to be taken into account apart from taste in order to increase consumption for older hospital patients
Acknowledgements

- Dr Maria Dermiki
- Students
  - J. Willway (MSc)
  - L. Binks (MSc)
  - J. Kidman (BSc)
  - C. Anderson (BSc)

- RBH NHS Trust Catering:
  W. Robinson, J. Fitzgerald, J. Swift

- RBH NHS Clinical:
  Professor of Elderly Care Medicine M. A. Gosney

- Heston Blumenthal
- Volunteers
- Sensory panel

Thank you
Muscle loss in old age: Is it all due to ageing?

Steve Harridge

BAPEN 2011
Some background thoughts on human ageing...

• Being physically active (and eating well) is the default position for maintaining good physiological function
  – “Exercise is not a mere variant of the condition of rest, it is the essence of the machine”. Barcroft, J. (1934)

• It follows that exercise should be not be viewed as a positive intervention, more that “sedentariness” is a negative intervention

• The effects of sedentariness are not predicable (but usually negative) and distort the effects of the inherent ageing process on physiological function

• Our understanding of the changes in physiological function due to ageing per se is incomplete, as we are unable to separate out inactivity factors from the inherent ageing process

Biological “ageing” or the study of “older people”?

Most studies of ageing err in this direction

Ageing + disuse ≠ ageing

Inactivity is deleterious to health and contaminates many studies of ageing. As such it confounds our understanding of the inherent biological ageing process
Some more background thoughts...

- We do not know the optimal type, intensity or volume of exercise needed to maintain good physiology throughout the lifespan.
- It is undoubtedly true that one type of exercise will not be optimal for all physiological systems and that specific exercise of one type may favour a particular system.
- The longitudinal study of individuals who maintain very high levels of physical activity will help us to understand more about inherent ageing on physiological function.
- This talk will consider primarily what we know about the muscles of “typical” older people.

Loss of strength in outwardly healthy older people

Skelton et al. (1994)
Age & Ageing

Dynapenia
Same torque requirement

Power deficit for the same torque

Harridge & Young (1996)
Data from Harridge & White (1993)
Implications of a decline in function

We should not assume this decline is linear

Muscle Function

Age

Threshold for independence

Loss of independence

Illness / Fall

Modified from Young (1995)
The main (but not only) problem....

Parise & Yarasheski (2000)
*Curr Opin Clin Nutr Metab Care,*
Functions of skeletal muscle:

- Biological machine
- Endogenous source of heat
- Dynamic metabolic store
- Protective padding
- Metabolic regulation
Specific Force Loss

The decline in isometric knee extensor force can be greater than the decline in quadriceps CSA

Young et al. (1985)
No specific force loss in endurance trained elderly

D’Antona et al. (2007)
Decline in specific force appears to relate to decreased activity

D’Antona et al. (2007)
Why are older muscles smaller?

Parise & Yarasheski (2000)
*Curr Opin Clin Nutr Metab Care,*

85 yr

31 yr

Sarcopenia
McComas (1996)

Lexell et al. (1988)
Old age is associated with fast fibre atrophy

<table>
<thead>
<tr>
<th>Study</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Muscle</th>
<th>Muscle fiber size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Type I</td>
</tr>
<tr>
<td>Snijders et al. (2009)</td>
<td>M</td>
<td>26 ± 1 vs 64 ± 1</td>
<td>gastrocnemius</td>
<td>←→</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>23 ± 1 vs 63 ± 1</td>
<td>gastrocnemius</td>
<td>←→</td>
</tr>
<tr>
<td>Dreyer et al. (2006)</td>
<td>M</td>
<td>21–35 vs &gt;60</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Frontera et al. (2008)</td>
<td>M/F</td>
<td>71 ± 5 vs 80 ± 5</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Kim et al. (2005b)</td>
<td>M/F</td>
<td>20–35 vs 60–75</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Kosek et al. (2006)</td>
<td>M/F</td>
<td>20–35 vs 60–75</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Larsson et al. (1978)</td>
<td>M</td>
<td>20–29 vs 60–65</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Lexell et al. (1988)</td>
<td>M</td>
<td>15–22 vs 80–83</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Petrella et al. (2006)</td>
<td>M</td>
<td>20–35 vs 60–75</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>20–35 vs 60–75</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
<tr>
<td>Sato et al. (1984)</td>
<td>F</td>
<td>≤39 vs ≥70</td>
<td>pectoralis minor</td>
<td>↑ (±8%)</td>
</tr>
<tr>
<td>Verdijk et al. (2007)</td>
<td>M</td>
<td>20 ± 1 vs 76 ± 1</td>
<td>vastus lateralis</td>
<td>←→</td>
</tr>
</tbody>
</table>
Fast fibre atrophy ameliorated by exercise

Vastus Lateralis mean fibre CSA ($\mu$m$^2$)

<table>
<thead>
<tr>
<th>Type</th>
<th>Young (20-30 years)</th>
<th>Old (Sedentary) (68 years)</th>
<th>Old (Endurance) (70 years)</th>
<th>Old (Strength) (68 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>4500</td>
<td>4400</td>
<td>4000</td>
<td>5200</td>
</tr>
<tr>
<td>Type IIa</td>
<td>6900</td>
<td>3800</td>
<td>4000</td>
<td>5500</td>
</tr>
<tr>
<td>Ratio</td>
<td>1.5</td>
<td>0.9*</td>
<td>1.0</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Klitgaard *et al.* (1990)
Master weightlifters

- **Absolute values**
  - **Age (Yrs)**: 0, 40, 50, 60, 70, 80, 90
  - **Weight lifted (kg)**: 0, 40, 60, 80, 100, 120, 140, 160, 180

- **Graph**:
  - Clean & Jerk
  - Snatch
  - 55kg
Modified Nottingham Power Rig

Pearson et al. (2001)
Lifters ~35% more powerful

Pearson et al. (2002)

Why are the mechanisms driving muscle loss?

Parise & Yarasheski (2000)
*Curr Opin Clin Nutr Metab Care,*

Sarcopenia
Candidates for Sarcopenia include...

- ↓ level of “anabolic” hormones
  - (e.g. GH/IGF-I, Testosterone, etc)
- Metabolic changes
  - (↑ reactive O₂ species)
- Inflammation and cytokines (“inflamageing”)
  - (↑ TNFα etc., ↑ degredation)
- Anabolic resistance to feeding and exercise
  - (↓ protein synthesis)
- ↓ regeneration from exercise induced damage
  - (compromised satellite cell behaviour)
Basal rate of protein synthesis unchanged in healthy elderly muscle

Fig. 1. Myofibrillar protein synthesis (means ± SD) in 31 young and 31 old men, all healthy normally physically active and none frail.

Rennie et al. (2010)
sensitivity of aged muscle to amino acids?

Cuthbertson et al. (2005)

FASEB
sensitivity of aged muscle to amino acids?

Cuthbertson et al. (2005)

FASEB
Post-prandial muscle protein synthetic response

Pennings et al. (2011)
sensitivity of aged muscle to exercise?

Kumar V et al. (2009)
J Physiol. 2009
Similar increases in muscle protein synthesis rates in young and old men and women

2 weeks (5 x per week)

Hasten et al. (2000)
Am J Physiol 278:E620-E626
Can we improve mass & function in older people?
Can we restore mass and function?

4 males 85 - 92 years
7 females 85 - 97 years

12 weeks - 3 times per week

3 x 6 x 80% 1-RM

Harridge et al. (1999)
Adaptations to strength training in very elderly people – similar to young

Harridge et al. (1999)
Very old muscle can hypertrophy

92 year old male

Harridge et al. (1999)
Muscle & Nerve
Table 2. Increases in leg strength obtained from high-intensity resistance training in the elderly

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Type of training</th>
<th>Duration</th>
<th>Effects observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bamman [63]</td>
<td>RCT, healthy</td>
<td>M/F</td>
<td>mean 69</td>
<td>3x/week @ 80% 1-RM</td>
<td>25 weeks</td>
<td>82% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Brose [65]</td>
<td>RCT, healthy, community-dwelling subjects</td>
<td>M/F</td>
<td>mean 66</td>
<td>3x/week @ 80% 1-RM</td>
<td>14 weeks</td>
<td>66% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Carmeli [87]</td>
<td>RCT, ambulatory nursing home residents</td>
<td>M/F</td>
<td>mean 82</td>
<td>2-5 kg free weights</td>
<td>12 weeks</td>
<td>10-15% ↑ in isokinetic leg strength</td>
</tr>
<tr>
<td>Charette [66]</td>
<td>RCT, healthy, community-dwelling subjects</td>
<td>F</td>
<td>mean 69</td>
<td>3x/week @ 65-75% 1-RM</td>
<td>12 weeks</td>
<td>28-115% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Connelly [73]</td>
<td>RCT, healthy, community-dwelling subjects</td>
<td>M/F</td>
<td>mean 76</td>
<td>3x/week concentric/ eccentric isokinetic ankle dorsiflexion @ max effort</td>
<td>2 weeks</td>
<td>15% ↑ in isokinetic ankle strength</td>
</tr>
<tr>
<td>Ferri [67]</td>
<td>no control group, healthy, physically active subjects</td>
<td>M</td>
<td>mean 68</td>
<td>3x/week @ 80% 1-RM</td>
<td>16 wk</td>
<td>27% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Frontera [60]</td>
<td>no control group, healthy, sedentary subjects</td>
<td>M</td>
<td>60-72</td>
<td>3x/week @ 80% 1-RM</td>
<td>12 weeks</td>
<td>107% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Frontera [68]</td>
<td>RCT, healthy, sedentary, community-dwelling subjects</td>
<td>F</td>
<td>mean 74</td>
<td>3x/week @ 85% 1-RM</td>
<td>12 weeks</td>
<td>39% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Fiatarone [61]</td>
<td>no control group, ambulatory nursing home residents</td>
<td>M/F</td>
<td>mean 90</td>
<td>3x/week @ 80% 1-RM</td>
<td>8 weeks</td>
<td>174% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Fiatarone [64]</td>
<td>RCT, ambulatory nursing home residents</td>
<td>M/F</td>
<td>mean 87</td>
<td>3x/week @ 80% 1-RM</td>
<td>10 weeks</td>
<td>37-178% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Lexell [62]</td>
<td>RCT, healthy, community-dwelling subjects</td>
<td>M/F</td>
<td>70-77</td>
<td>3x/week @ 85% 1-RM</td>
<td>11 weeks</td>
<td>163% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td>Roth [69]</td>
<td>RCT, healthy, sedentary community-dwelling subjects</td>
<td>M/F</td>
<td>mean 25</td>
<td>3x/week @ 100% 5-RM</td>
<td>1st 13 weeks</td>
<td>5.9% ↑ in thigh muscle volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M/F</td>
<td>mean 69</td>
<td>3x/week @ 100% 15-RM</td>
<td>2nd 13 weeks</td>
<td>5.0% ↑ in thigh muscle volume</td>
</tr>
<tr>
<td>Vincent [72]</td>
<td>RCT, healthy, sedentary community-dwelling subjects</td>
<td>M/F</td>
<td>mean 68</td>
<td>3x/week @ 50% 1-RM</td>
<td>24 weeks</td>
<td>16% ↑ in 1-RM leg strength</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M/F</td>
<td>mean 67</td>
<td>3x/week @ 80% 1-RM</td>
<td>24 weeks</td>
<td>20% ↑ in 1-RM leg strength</td>
</tr>
</tbody>
</table>

RCT = randomized controlled trial.
Candidates for Sarcopenia include...

- ↓ level of “anabolic” hormones
  - (e.g. GH/IGF-I, Testosterone, etc)
- Metabolic changes
  - (↑ reactive O₂ species)
- Inflammation and cytokines (”inflamageing”) 
  - (↑ TNFα etc., ↑ degradation)
- Anabolic resistance to feeding and exercise
  - (↓ protein synthesis)
- ↓ regeneration from exercise induced damage
  - (compromised satellite cell behaviour)
Parabiotic mice – conjoined circulation

Conboy et al. (2005)
Satellite cell “niche” regulates satellite cell behaviour

Local environment influencing satellite cell includes:
- Blood
- Extra cellular matrix
- Interstitial fluid
- Adjacent myofibres
Comparable studies in humans??

Parabiotic pairing?

![Diagram showing parabiotic mice with young and old mice, and the process of generating and injuring leg muscles, with resulting regenerated and impaired regeneration.](image-url)
In vitro model of muscle & systemic milieu
In vitro human muscle / circulatory system

1. Obtain sample of muscle from young and elderly people

2. Obtain serum from young & elderly people

3. Culture cells (myoblasts)
Human myoblasts cultured in human serum

Cells stained with antibodies to desmin (muscle, green) and Ki-67 (proliferating cells, pink) and nuclei (blue).
Effects of serum age on myoblast proliferation

6- Young (aged 22 - 26)

Young Serum

(3, 5 & 7 days culture in 15% serum)

(1 Young Cell population)

6 - Elderly (aged 80-82)

Elderly Serum

Cells
No effect of serum age on proliferation at D5

George et al. (2010)
Experimental Gerontology
No effect of age of cell donor on differentiation

Alsharidah et al.
In preparation
Muscle mass, strength and power decline with increasing age. This is associated with decreased physical function and an increased risk of falls.

The rate at which loss occurs due to “ageing” is difficult to identify due to:
  - Inappropriate cohorts which confound interpretation of biological ageing
  - Reliance on cross-sectional studies

Muscle is sensitive to disuse, but there is an inherent ageing effect, as those who maintain high levels of physical training show a declines in function.

Anatomically muscle loss appears to be due to a loss of muscle fibres (motor units) & the atrophy of type II fibres.
Older peoples muscles may exhibit “anabolic resistance” to feeding and exercise

Human muscles satellite cells show no age related impairment in behaviour

High resistance training is the most effective means for improving muscle mass and function in older people
Strength training: the elixir of muscle youth?

Harridge & Saltin (2007)
Encyclopaedia of Gerontology

Move to a new “slope”, but with similar rate of decline?

Years of “functional” gain

Muscle Strength

Threshold for independence

Age

Training
Acknowledgements

Norman Lazarus
Cristiana Velloso
Tomasz George
Mansour Alsharidah
Chibeza Agley

Steve Pearson
Mahjabeen Hameed
Matt Cobbold
Richard Orrell
Roger Woledge
Archie Young

Bengt Saltin
Ann Kryger
Michael Kjaer
Jesper Andersen
Peter Schjerling
Ageing and the gut

John McLaughlin
Manchester University/
Hope Hospital, Salford UK
Nutrition and age

- Reduced Intake
- $\downarrow$ Absorption
- $\downarrow$ Utilisation

Consequences: see other lectures
Nutrition and age

- Reduced Intake
- $\downarrow$ Absorption
- $\downarrow$ Utilisation

WHAT DO WE KNOW?

impaired nutrition
REALLY, most problems arise before anything needs absorption in the gut...

- Poverty, poor mobility, isolation, cognitive loss...
- Dry mouth
  - drugs
- Dentition and dentures
- Weak mastication
- Sore mouth
- Anorexia/nausea
- Dysphagia
  - Oropharyngeal
    - Neurological?
  - Oesophageal
    - Motility
    - Stricture
    - Cancer
    - Candida
    - Reflux
Gut function broadly preserved with healthy ageing

- Limited impact on nutrition if feeding is maintained
- GI diseases prevalent in the elderly
Animals are designed for survival

Maximal absorption of nutrients is essential – Biological and evolutionary pressure is of food scarcity – And not cooked/processed/biologically safe – So human gut is highly over-efficient

Age is not a major limitation in health…Gut epithelium self-replaces every 4-7 days so no 'wear and tear' ageing Not so for muscle/nerve/immune cells
Gut has 2 conflicting roles

• Digestion and absorption: get food and water in

  » Versus

• Barrier function: keep microbes and toxins out

Do these change with age?
Ageing and the stomach 1

- Hypochlorhydria: *reduced acid*
  - Atrophic gastritis/surgery
  - H. pylori principally responsible, not age
    (high % prevalence is a cohort effect of Hp acquired in childhood)
  - PPI/H$_2$RAs

Predispose to *bacterial overgrowth*
Ageing and the stomach 2

• Hypochlorhydria: reduced acid
  - Reduced iron absorption
  - Reduced B12 absorption also in atrophic gastritis/PA
    • Intrinsic factor loss
Gastric acid secretion

Epithelium

Lumen

Epithelium

H+

H+ (pH < 3.5)

H+

Histamine

Gastrin

Somatostatin

parietal

ECL

G-cell

D-cell

Stretch/
Amino acids

+ + +
Achlorhydria

H. pylori, autoimmunity, drugs

Histamine

Gastrin: Increased by loss of negative feedback

GI CANCER RISK FACTOR?
Gastric emptying

- Increasingly slow with age
  - eg increased CCK responses with age
- May potentiate sensation of satiety post-prandially
  - Persistent gastric distension: full for longer
  - Slower delivery of nutrients prolonging intestinal satiety signals
  - Sentisised sensory nerve endings in inflammation
  - Altered neuropeptide signalling
- Nitrite etc formation enhances UGI cancer risk?
Satiety
Nausea/Vomiting
Hormones
+ve
Vagus

ENS

Spinal Cord

PAIN

Arrows indicate the direction of influence between various components of the autonomic nervous system and pain perception.
Motility and age

• **Gastric emptying slows**
  - Drug delivery consequences

• **Small bowel motility: largely preserved unless intercurrent disease**
  - Diabetes, Drugs, Hypothyroidism...

• **Colonic transit tends to slow**
  - ↑ water absorption, ↑ constipation...
  consequent symptoms
Transport and absorption

Epithelium
(enterocytes)

Transcellular

Paracellular

Lumen

X = tight junction

X = tight junction
Ageing has little impact on small bowel nutrient transport

- Villus/crypt architecture preserved
- Reduced transporter molecules/mg bowel
- But little evidence for absorptive organs ‘simply’ failing with age:
  - Small intestine has reserve capacity++
  - Absorption time probably prolonged
  - eg 72 hour faecal fat excretion not affected by age

And if fat can be absorbed, anything can...
Small bowel is lined by highly adapted cells

- Differentiation from crypt stem cells
  - Absorptive enterocytes (~90%)
    - Transporters +++
    - TRANSPORT DEFECTS UNLIKELY TO CONTRIBUTE TO SARCOPAENIA
    - Calcium/zinc absorption maybe age limited
  - Secretory cells also (~10%)
    - Endocrine (as previous talk)
    - Goblet cells (mucus: reduced in age)
    - Paneth cells (defence: age effects unclear)
Gut diseases cause malabsorption in the elderly

- Enterocyte loss or damage
  - Bacterial overgrowth
    - Jejunal diverticulosis
  - Flat mucosa of any cause:
    - villous atrophy inc coeliac
  - Ischaemia
  - Crohn’s
  - Drugs
Gut diseases cause malabsorption in the elderly

- **Pancreatic/biliary insufficiency:** fat and fat soluble vitamins
- **Fistulas and short bowel:** increasingly common in the elderly as access to safe surgery / anaesthesia have become less age restricted
Ageing and the gut

• Adaptation after injury is impaired
  - Surgery
  - Infection/inflammation
  - Radiotherapy

• Adaptation normally driven by
  - Growth factors (EGF, KGF, trefoil peptides)
  - GLP-2 via enteric neuronal plexuses
    • Targets?
Normal epithelium depends on immune/bacterial interactions

- Gnotobiotic (germ free) animals
  - Mice
  - Zebra fish

\[\text{Reduced crypt proliferation, abnormal enterocytes}\]

- T cell receptor $\alpha$ knockout mice: reduced endocrine cell numbers
Human beings as ‘metaorganisms’

‘...derived from millennia of co-evolution with their own indigenous intestinal microbiota. In the light of the metaorganism hypothesis a more holistic view of the process of human ageing has been suggested where the ageing of the microbial counterpart is regarded as important’. Biagi 2010
Microbiome

• Diversity++
  - Colonised at birth
  - Stability?

• Should we look at faecal or adherent bugs?

• Loss of diversity observed *eg* in IBD
Microbiome: ageing effects?

- Limited and conflicting data
- No global or consistent change
- Increased pathobiont numbers
  - eg Staphylococci, Enterococci
- Reduced numbers/diversity of Bifidobacteria sp
  - 'Health promoting'
- Magnified by antibiotic use
  - C. difficile
- Prebiotics/probiotics?
Immunosenescence

- Age related reduction in
  - gut-associated lymphoreticular tissues
  - intestinal antigen-specific IgA antibody secretion
  - T-cell function

GI infections
Morbidity and mortality
Immune system tolerates gut bacteria

• Normal proximal GI tract is not sterile
  - Stomach: $10^4$ cfu/g
  - Small bowel: jejunum $10^5$-$10^7$ cfu/g; ileum $10^7$-$10^8$
  - Colon: $10^{10}$-$10^{11}$

  *cfu: colony forming units*

• Small bowel overgrowth:
  - Defective mucosal immunity
  - Hypo/achlorhydria
  - Diverticulosis
  - Fistulae, strictures
  - Stasis: hypomotility
Is B.O.G. important?

• 490 elderly inpatients
• 11% malnourished
  ...of whom 44% had occult malabsorption
  ...of whom 71% had B.O.G.
• Antibiotics lead to weight gain, rise in Hb, rise in protein/Ca++
• But also find B.O.G. in healthy old people with no malabsorption
What is the mechanism of malabsorption in B.O.G.?

- Enterocyte damage
  - Fused microvilli
  - Endoplasmic reticulum abnormalities
  - Reduced glucose uptake in isolated brush border vesicles
- Brush border enzyme loss
- Bile salt deconjugation
- Inflammation: ↑ IL6
Transport and absorption

Transcellular

Epithelium
(enterocytes)
Immune Barrier

Epithelium
(enterocytes)

Antigens/ Microbes/ Drugs

X = tight junction
Paracellular pathway is leaky in inflammation/malnutrition.

**Diagram:***
- **Transcellular** pathway involves crossing the epithelium (enterocytes) directly.
- **Paracellular** pathway involves crossing the tight junctions (X) which are leaky in inflammation/malnutrition.
- Antigens can bypass the tight junctions and enter the lumen directly.

**Legend:**
X = tight junction
'Inflamm-aging'

May drive age related pathology eg sarcopenia, neurodegeneration?

Gut microbiome/immunity/leakiness could be key factors
Concluding speculation

- Neuroendocrine changes
  - reduced appetite

- Microbiome modification or bacterial overgrowth

- Reduced barrier function

All contribute to systemic inflammatory/metabolomic responses?
Thank you
An investigation the relationship between nutritional risk of elderly patients with dementia and behavioural problems at mealtimes for patients with dementia.

M.Mc.Keon¹,², S.Faherty², C.Glennon¹, G. Flanagan-Rughoobur¹, M.ORegan³ and M.McDonnell-Naughton²

¹Community Nutrition & Dietetics Service, Health Service Executive Dublin Mid-Leinster, Republic of Ireland,
²Department of Nursing and Health Science, Athlone Institute of Technology, Republic of Ireland,
³Department of Statistics, Trinity College Dublin, Republic of Ireland.
Currently there are almost 44,000 people in Ireland with dementia.

It is estimated this number will double and in thirty years it will treble making dementia is one of the most important health issues of our time.

(Alzheimer's society of Ireland 2011)
Background

People with dementia may suffer from anorexia, under nutrition and involuntary weight loss (Aselage MB & Amella EJ 2010).

Studies indicate that unintentional weight loss may increase mortality and reduce resistance to infections (Barker L, Gout BS & Crowe TC, 2011).
Background

Feeding difficulties have been identified as one of the main factors that contribute to weight loss and poor nutritional status in people with dementia

(Dunne A. 2010)
Background

Previous research has looked into the behaviours that patients exhibit when eating but it is not known how these behaviours are related to nutritional status.
Aim of study

This study aims to examine the frequency of feeding difficulties seen among older people with dementia in a primary care setting in the Republic of Ireland.
Aim of study

- It also investigates if these difficulties are related to the nutritional status
Methodology
Assessment of nutritional risk

**MUST**

**Step 1** Body mass index score
- 0: Normal
- 1: Underweight
- 2: Obese

**Step 2** Weight loss score
- Unplanned weight loss in past 3-6 months
  - % Score
  - <5 0
  - 5-10 1
  - >10 2

**Step 3** Acute disease effect score
- If patient is acutely ill and there has been or is likely to be no nutritional intake for >15 days Score 2

**Step 4** Overall risk of malnutrition
- Add scores together to calculate overall risk of malnutrition
  - Score 0 Low risk
  - Score 1 Medium risk
  - Score >2 High risk

**Step 5** Management guidelines
- **0 Low risk** Routine clinical care
  - Repeat - weekly
  - Hospital - weekly
  - Care homes - monthly
  - Community - annually for special groups, eg, patients >75 years

- **1 Medium risk** Observe
  - Document dietary intake for 3 days if patient in hospital or care home
  - If improved or adequate intake - little clinical concern; if no improvement - clinical concern - follow local policy
  - Repeat screening
  - Hospital - weekly
  - Care home - at least monthly
  - Community - at least every 2-3 months

- **2 or more High risk** Treat*
  - Refer to dietitian, nutritional support team or implement local policy
  - Improve and increase overall nutritional intake
  - Monitor and review care plan
  - Hospital - weekly
  - Care home - monthly
  - Community - monthly
  - *Unless detrimental or no benefit is expected from nutritional support, eg, imminent death

**MNA**

Mini Nutritional Assessment MNA®

<table>
<thead>
<tr>
<th>Screening score</th>
<th>0-3 points</th>
<th>4-7 points</th>
<th>8-11 points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk</strong></td>
<td>Low</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td><strong>Nutritional</strong></td>
<td>Poor</td>
<td>Poor</td>
<td>Poor</td>
</tr>
<tr>
<td><strong>Support</strong></td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not needed</td>
</tr>
</tbody>
</table>

*Screening score: 0-3 points: Low risk; 4-7 points: Medium risk; 8-11 points: High risk; *Unless detrimental or no benefit is expected from nutritional support, eg, imminent death.
Methodology

The Edinburg Feeding and evaluation questionnaire (ED-FED-Q) was used to categorise and measure behavioural problems at mealtimes.

(Watson & Keller, 2006)
Results

Eight seven percent (87/100) of patients who met the study criteria (i.e. greater than 65 years old with a diagnosis of dementia) were deemed eligible and consented to take part in the study.
# Results

Table 1: Results of the ED-FED Questionnaire (5)

<table>
<thead>
<tr>
<th>ED-FED Questionnaires Results**</th>
<th>Never n %</th>
<th>Sometimes n %</th>
<th>Often n %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the patient require close supervision while eating?</td>
<td>4 5</td>
<td>41 47</td>
<td>42 48</td>
</tr>
<tr>
<td>Does the patient require physical help while feeding?</td>
<td>6 7</td>
<td>39 45</td>
<td>42 48</td>
</tr>
<tr>
<td>Is there any spillage while feeding?</td>
<td>9 10</td>
<td>45 52</td>
<td>33 38</td>
</tr>
<tr>
<td>Does the patient leave food on the plate?</td>
<td>33 38</td>
<td>23 27</td>
<td>31 36</td>
</tr>
<tr>
<td>Does the patient ever refuse to eat?</td>
<td>36 41</td>
<td>28 32</td>
<td>23 27</td>
</tr>
<tr>
<td>Turn head away while being fed?</td>
<td>37 43</td>
<td>27 31</td>
<td>23 26</td>
</tr>
<tr>
<td>Refuse to open mouth?</td>
<td>41 47</td>
<td>31 36</td>
<td>15 17</td>
</tr>
<tr>
<td>Spit out food?</td>
<td>47 54</td>
<td>22 25</td>
<td>18 21</td>
</tr>
<tr>
<td>Leave mouth open (leaving food to drop out)?</td>
<td>45 52</td>
<td>27 31</td>
<td>15 17</td>
</tr>
<tr>
<td>Refuse to swallow?</td>
<td>53 61</td>
<td>25 28</td>
<td>9 10</td>
</tr>
</tbody>
</table>

*Note percentages are rounded off to the nearest whole number

**An ED-FED score of 10 or more indicates a high level of behavioural problems.
Results

The Ed FED-Q was found to be significantly correlated with both the ‘MUST’ and the ‘MNA’ categories of nutritional risk (P<0.01).
Results

- 80% (28/35) of participants who were categorised at high risk of malnutrition according to the ‘MUST’ had an Ed-FED score of >10.

- There is a negative linear relationship between the ‘MNA’ and the Ed-FED (r=-.706, P<0.01).
Conclusions

There is an important relationship between feeding difficulties and risk of malnutrition among elderly people with dementia.
Conclusions

- Malnutrition has negative effects to the individual in terms of clinical outcome and quality of life.

- The negative clinical outcome in turn increase health service utilisation costs significantly.
Conclusions

- It is therefore imperative that behavioural problems at mealtimes that are related to malnutrition be closely scrutinized, and considered.

- Especially when planning nutritional intervention, training and policy.
Acknowledgements

- Dr. Mary Mc Donnell- Naughton
- Dr. Shelia Faherty
- Dr. Myra O Regan
- Ms. Corina Glennon
- MS. Grainne Flanagan Rughoobur