Fertility Challenges – Is the male part of the treatment? 
*The other half of the subfertile hemisphere.*
Fertility Rates 1960–2013,
Skakkebaek et al. 2016

North America
- Canada
- Mexico
- USA
- Replacement level

Africa
- Egypt
- Ethiopia
- Libya
- Morocco
- Somalia
- South Africa
- Sudan
- Zimbabwe
- Replacement level

South America
- Argentina
- Bolivia
- Brazil
- Chile
- Colombia
- Ecuador
- Paraguay
- Peru
- Uruguay
- Venezuela
- Replacement level

Europe
- Denmark
- Finland
- France
- Germany
- Greece
- Netherlands
- Norway
- Portugal
- Spain
- Sweden
- United Kingdom
- Replacement level
AGE AT FIRST DELIVERY

![Graph showing the age at first delivery in Germany, West Germany, and East Germany from 1991 to 2003.](image)
DOES MALE FERTILITY DECREASE?

Opinions seem controversial.

Overview of publications shows decline of sperm quality.
DECREASE IN SPERM QUALITY

Swan et. al. – National Institute of environmental health sciences

• Review of 61 published studies
• Data collected over 52 years (1938 to 1990)
• Decline in average sperm density in U.S. and other Western countries

Average annual decrease of

U.S. 1.5 mio/ml = minus 1.5%/year

Europa minus 3.1%/year
DECREASE IN SPERM QUALITY

Lackner et al. 2007 Fertility & Sterility

9327 men within the last 18 years

Results:

**Age** 30.8 rised to 34.4

**Sperm count** 27.75 to 4.60 mio/mL
DECREASE IN SPERM QUALITY

**FIGURE 11.** Distributions of sperm counts in Danish men from the general population, examined from 1996 to 2010 and Danish men examined in an infertility clinic in the 1940s. All men had durations of ejaculation abstinence greater than 48 h. Sperm concentration (A) and total sperm counts (B) are shown. [From Jørgensen et al. (189).]
DEVELOPMENT OF SEMEN QUALITY

[Graph showing the development of semen quality in the USA, Europe, and Non Western countries from 1935 to 1995. The graph indicates a decrease in sperm density (millions/ml) over time.]
THERAPY OF MALE SUBFERTILITY

- **Kinin-enhancing drugs** for unexplained subfertility in men. Vandekerckhove et al. Cochrane Database 2000(2)

- **Androgens** versus placebo or no treatment for idiopathic oligo/asthenospermia. Vandekerckhove et al. Cochrane Database 2000(2)

- **Clomiphene or tamoxifen** for idiopathic oligo/asthenospermia. Vandekerckhove et al. Cochrane Database 2007 Jul 18;(4)

- **Surgery or embolisation for varicocele** in subfertile men. Evers JL, Collins JA. Cochrane Database Syst Rev. 2004;(3)
MALE SUBFERTILITY AND NUTRITION

Reduction of Sperm Quality

• No Disease?
• Defiency Syndrom?

Could therapy be Supplementation?
LACK OF MICRONUTRIENTS IN FOOD

Guidelines on food fortification with micronutrients
Lindsay Allen et al.
World Health Organization
2006

Male factor subfertility: possible causes and the Impact of nutritional factors.
Wong WY et al.
LACK OF MICRONUTRIENTS IN FOOD

Worldwide, approximately 2 billion people are affected by Hidden Hunger.

Global Hidden Hunger Map

SIGHT AND LIFE

MEDICAL UNIVERSITY OF VIENNA
**MALE SUBFERTILITY AND NUTRITION**

**Micronutrients in food 1985, 2002**

<table>
<thead>
<tr>
<th>Mineralien und Vitamine in mg je 100 g Lebensmittel</th>
<th>untersuchte Inhaltsstoffe</th>
<th>Ergebnis 1985</th>
<th>Ergebnis 1996</th>
<th>Ergebnis 2002</th>
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</thead>
<tbody>
<tr>
<td><strong>Brokkoli</strong></td>
<td>Calcium</td>
<td>103</td>
<td>33</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Folsäure</td>
<td>47</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Magnesium</td>
<td>24</td>
<td>18</td>
<td>11</td>
</tr>
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<td><strong>Bohnen</strong></td>
<td>Calcium</td>
<td>56</td>
<td>34</td>
<td>22</td>
</tr>
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<td></td>
<td>Folsäure</td>
<td>39</td>
<td>34</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Magnesium</td>
<td>26</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Vitamin B 6</td>
<td>140</td>
<td>55</td>
<td>32</td>
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<tr>
<td><strong>Kartoffeln</strong></td>
<td>Calcium</td>
<td>14</td>
<td>4</td>
<td>3</td>
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<tr>
<td></td>
<td>Magnesium</td>
<td>27</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td><strong>Möhren</strong></td>
<td>Calcium</td>
<td>37</td>
<td>31</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Magnesium</td>
<td>21</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td><strong>Spinat</strong></td>
<td>Magnesium</td>
<td>62</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Vitamin C</td>
<td>51</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td><strong>Apfel</strong></td>
<td>Vitamin C</td>
<td>5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Banane</strong></td>
<td>Calcium</td>
<td>8</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Folsäure</td>
<td>23</td>
<td>3</td>
<td>5</td>
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<tr>
<td></td>
<td>Magnesium</td>
<td>31</td>
<td>27</td>
<td>24</td>
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<tr>
<td></td>
<td>Vitamin B 6</td>
<td>330</td>
<td>22</td>
<td>18</td>
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<tr>
<td><strong>Erdbeeren</strong></td>
<td>Calcium</td>
<td>21</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Vitamin C</td>
<td>60</td>
<td>13</td>
<td>8</td>
</tr>
</tbody>
</table>

**Ursache:** Ausgelaugte Böden, Luftverschmutzung, zu schnelles Wachstum

*Quelle: 1985 Pharmakonzern Geigy (Schweiz). 1996 Lebensmittellabor Karlsruhe/Sanierung*
DECREASE IN SPERM QUALITY

Antioxidant intake is associated with semen quality in healthy men.


CONCLUSIONS:

... higher antioxidant intake was associated with higher sperm numbers and motility ...
SPERMIOGENESIS

Spermiogenesis

Day 1  Day 18  Day 36  Day 54  Day 72
## EFFECTS ON SPERMI OGENESIS

<table>
<thead>
<tr>
<th>PROfertil® composition²</th>
<th>Impact on male fertility-related factors³-⁷</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ingredient</strong></td>
<td><strong>Dose per day</strong>&lt;br&gt;(2 capsules)</td>
</tr>
<tr>
<td>L-Arginine</td>
<td>250 mg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>120 mg</td>
</tr>
<tr>
<td>Folic acid</td>
<td>800 mcg</td>
</tr>
<tr>
<td>Selenium</td>
<td>60 mcg</td>
</tr>
<tr>
<td>Glutathione</td>
<td>80 mg</td>
</tr>
<tr>
<td>Coenzyme Q10</td>
<td>15 mg</td>
</tr>
</tbody>
</table>
STUDY MEDICATION

2x1 Capsule daily for 3 Month

- L-Carnitine 440 mg
- L-Arginine 250mg
- Vitamin E 120 mg
- Folic-acid 800 μg
- Zinc 40 mg
- Selenium 60 μg
- Glutathione 80 mg
- Coenzyme Q10 15 mg

The European e-Journal of Clinical - Nutrition & Metabolism 12/2011
STUDY SETTING

Therapy Group  132 men, age Ø 34 a (18-43)

2 Capsules/day  MICRONUTRITIENTS (Profertil)
for 3 month

Control Group  73 men, age Ø 38 a (22-52)

No TREATMENT / CHANGE OF LIFE STYLE

The European e-Journal of Clinical - Nutrition & Metabolism 12/2011
DESIGN

2 path spermiogr.

Treatment group
Profertil 2 capsules

Control group
Change life style

Observation period

End of study

Questionare

Telephone
Follow up

12 month
Inclusion

3 month
Study period

6 month
Follow up

The European e-Journal of Clinical - Nutrition & Metabolism 12/2011
RESULTS THERAPY GROUP

**Ejaculate in ml**
- 3.5 ml
- 2.9 ml
- 2 ml
- 1.5 ml

**Concentration in Mio/ml**
- 18 mio
- 20 mio
- 15 mio

**Morphology**
- 40%
- 29%
- 30%
- 4%

**Comparison**
- Ejaculate: +33.3% p<0.5
- Concentration: +215% p<0.5
- Morphology: +23% P<0.5
THERAPY COMPARED TO CONTROL

- Therapy Group
- Control Group

Bar chart showing comparisons:
- Volume %
- Density %
- Fast forward %
- Total movement %
- Morphology %
**IMPROVEMENT WITH MICRONUTRIENTS AFTER 3 MONTH**

After 3 month treatment

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>132</td>
<td>73</td>
</tr>
<tr>
<td>34 preg.(25.8%)</td>
<td>11 preg.(15.1%)</td>
</tr>
</tbody>
</table>
Patient, 41a, after 3 month of treatment.

Patient, 33a, after 3 month of treatment.
Improvement of sperm quality after micronutrient supplementation

Martin Imhofa,b,*, Jakob Lacknera,c, Markus Lipovaca,b, Peter Chedrauid, Claus Riedle
Improvement of Sperm Quality in Patients with Subclinical Varicocele
Improvement of Sperm Quality in Patients with Subclinical Varikocele

**Initial-Situation**
55 men, drop out 4, Ø 32 year, (18-43)

**Inclusion - criteria**
Infertility for > 2 years (Ø 2,7 years)
Pathological Spermiogram
Subclinical Varikocele

**Exclusion - criteria**
Infection, Aspermia, hormonal disorder
# RESULTS AFTER 3 MONTH

<table>
<thead>
<tr>
<th></th>
<th>Prä</th>
<th>Post</th>
<th>Δ%</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume</strong></td>
<td>3,21</td>
<td>3,71</td>
<td>12,5%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Density</strong></td>
<td>56,53</td>
<td>63,25</td>
<td>15,6%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Fast Forward</strong></td>
<td>14,59</td>
<td>20,97</td>
<td>43,8%</td>
<td><strong>signif. p&lt; 0,05</strong></td>
</tr>
<tr>
<td><strong>Total Motility</strong></td>
<td>50,35</td>
<td>58,37</td>
<td>16,1%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
<td>22,39</td>
<td>26,47</td>
<td>18,2%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Preg (6 month)</strong></td>
<td>21</td>
<td>41,20%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
EFFECT OF MICRONUTRIENTS


Antioxidants for male subfertility.
Showell et al.

AUTHORS' CONCLUSIONS: The evidence suggests that antioxidant supplementation in subfertile males may improve the outcomes of live birth and pregnancy rate for subfertile couples undergoing ART cycles....
DNA Fragmentation


Saleh ED; Increased sperm nuclear DNA damage in normozoospermic infertile men: a prospective study.

CONCLUSION(S): ..... a significant increase in DNA damage can be found in sperm from infertile men with normal standard sperm parameters ............
DNA Fragmentation

Ribas-Maynou J, Double stranded sperm DNA breaks, measured by Comet assay, are associated with unexplained recurrent miscarriage in couples without a female factor.

Conclusion: ..... sperm DNA breaks are related to the paternal risk of having recurrent pregnancy loss .....
Can supplementation of micronutrients protect the DNA structure during human reproduction?
SPERM DNA FRAGMENTATION INDEX DECREASES AFTER MICRONUTRIENT SUPPLEMENTATION

Therapy Group 67 men, age Ø 39 a (24-48)

2 Capsules/day MICRONUTRITIENTS for 3 month

Control Group 40 men, age Ø 37 a (26 – 50)

No active TREATMENT

Main outcome measure was change in sperm-hyaluronan binding assay indicating DNA fragmentation after 3 months.
Results

Therapie micronutrienten Profertil

- 74%
- 56%

(p<0.05)

Control No Therapy

- 69%
- 64%

(p=0.083)
SIGNIFICANT REDUCTION OF DNA FRAGMENTATION

< 15% normal
15-30% IUI necessary
> 30% ICSI necessary
Micronutrients intake is associated with improved sperm DNA quality in older men.


PATIENT(S): 22-80-year-old nonsmoking men (n = 80)

CONCLUSION(S): Men with higher dietary and supplement intake of certain micronutrients may produce sperm with less DNA damage, especially among older men.
Figure 1. The relationship between age in years and semen volume (A), concentration (B), count (C), sperm motility (D), progressive motility (E) and total progressively motile sperm (F).

A combination of eight micronutrients is superior to 1000mg L-carnitin with respect to impaired sperm motility

- Men 18-60 years
- subfertility > 1 year
- At least one recent pathologic semen analysis (WHO 2010)

- Group 1: 144 men 1000mg L-carnitin
- Group 2: 127 men combination of 8 micronutrients

Both therapies increased semen motility significantly. The combination supplement was significantly superior in improvement of progressive and total motility.
Study Results

- Sperm Cell Density (mill/ml)
- Ejaculatory Volume (ml)
- Progressive Motility (%)
- Total Motility (%)
- Normal Morphology (%)

Improvement in %
- Treatment Group
- Control Group
- WHO Lower Limits 1998
RESULTS

• Both therapy groups semen motility to a highly significant level (p <0,001)

• The combined therapy increased rapidly progressive motile sperms highly significantly (p=0,004)

• Overall progressive sperm count significantly (p=0,01) compared to the mono-substance group.

• No major side effects
A combination of eight micronutrients is superior to a mono preparation comparing improvement of variant groups of impaired sperm motility

- Bodner F (Speaker), Lipovac M, Imhof M
CONCLUSION

Sperm quality and male fertility is decreasing

Decline of sperm quality seems a deficiency syndrome

Micronutrients are lacking in food

Micronutrients improve sperm quality in literature
CONCLUSION

Micronutrients significantly improve sperm quality.

Combination is superior over monotherapy.

Micronutrients improve DNA quality in sperm.

DNA quality can influence fertility and pregnancy.
TREATMENT POLICY

4 groups of patients

1. Male with impaired sperm quality

2. Male of a couple in treatment (eg. IUI, IVF, ICSI, IMSI, low dose stim.)

1. Subfertility of unknown reason > 6 Month

2. Male > 35 years
Austrian Governmental Scientific Society
Medical University of Vienna & Krems
THANK YOU TO ALL OUR PATIENTS AND

Markus Lipovac  
Johannes Barta  
Marianne Imhof  
Claus Riedl  
Jakob Lackner  
Peter Chedraui  
Bettina Pusker  

Erik Huber  
Florian Bodner  
Doris Peczar  
Margarete Karimi  
Christine Grünhut  
Rene Detter  
Natalie Steffl  

[Images of portraits for each person]
THANK YOU FOR YOUR ATTENTION