Berücksichtigung der Bioverfügbarkeit bei der Ableitung der RDAs

Consideration of bioavailability in the derivation of RDAs

Prof. Dr. Helmut Heseker
Universität Paderborn
Overview

- Introduction
- D-A-CH-Reference-Values (DRV)
- General considerations on deriving DRV
- Zinc
- Iron
- Concluding remarks
Since year 2000 the D-A-CH-Reference Values are valid for the German speaking countries. The DRV are developed by the German Nutrition Society (DGE) in cooperation with the Austrian (ÖGE) and Swiss (SGE) nutrition societies.

- **primary focus:** nutritive aspects and the prevention of deficiency
- **other preventive aspects** were also taken into consideration
- **up to now:** 2 minor revisions have been made
- **present situation:** a complete revision is in progress
Dietary Reference Values
Differentiation between recommendations, estimated values and guiding values

- **Recommendations** (*empfohlene Zufuhr*): Average requirement increased by two standard deviations assuming a normal distribution. If lack of normal distribution of values, the average requirement can be increased by 20–30% *(assuming a coefficient of variation of 10–15%)*

- **Estimated values** (*Schätzwert*): In case, human requirements cannot be determined with desirable accuracy, estimated values are still experimentally supported and provide appropriate information for adequate and safe intake.

- **Guiding values** (*Richtwert*): Aims to orient intake regulations if they are necessary for human health *(lower limit for water, fluoride, dietary fibre and upper limit for fat, cholesterol, alcohol and table salt)*.
List of nutrients for which DRV have been established

* The essentiality is still controversial.
The trace element requirement

Definition of **basal requirement** (WHO/FAO, 1996)
Target group: **healthy adults**

The **basal requirement** refers to the intake of trace elements needed to prevent pathologically relevant and clinically detectable signs of impaired functions attributable to inadequacy of the nutrient.

- Shows a wide variation.
- The determination in individual cases is difficult.
Dietary reference values process for trace elements

1. Assessment of the nutrient function.
2. Description of status indices.
3. Definition of criteria for adequacy and excess.
4. Measurement/estimation of the physiological requirement (e.g., daily losses).
5. Estimation of the dietary bioavailability.
6. Set DRV, UL for specific groups (sex, age, pregnancy..).
7. Implementation of DRV in food-based dietary guidelines, assessment of diets, ...
8. Identifying knowledge gaps, reviewing the literature to identify new data → revision of DRV.
Classical methods for the determination of nutritional requirements

- **Deficiency experiments on humans**
  (→ long-lasting, heavy burden to subjects, ethically questionable)
- **Tracer studies** with isotopes or radioactive substances
  (→ expensive, ethically questionable)
- **Balance studies** with stable nutrients (replacement of estimated daily excretion and losses → applicable for trace elements)
- **Factorial methods** (e.g. interpolation for children from adult data sets or derivation from breast milk)
- **Measurement of nutrient concentrations** in body fluids and tissues at specified amounts of nutrients (→ only possible in not homoostatic regulated nutrients)
- **Biochemical markers**: e.g. specific enzymes for selenium
- **Biological markers**: e.g. iodine and thyroid hormones
- **Animal experiments**: limited strength (different growth and survival rates, ..), but suitable to identify essentiality
Bioavailability of trace elements (1)

- total amount / dosage
- type of trace element compound
  (e.g. iron fumarate, iron oxide)
- binding form in food
  (e.g. phytate, oxalate)
- type of food
  (animal or plant origin)
- food processing
  (e.g. dough processing)
Bioavailability of trace elements (2)

- effectivity of the digestion
  *(e.g. hydrochloric acid, digestive enzymes)*
- interaction with other trace elements
- trace element supply status
- mechanism of the absorption
- presence of concomitants
  *(e.g. ascorbic acid, amino acids)*
- kind of transport mechanism
Deriving a DRV for a trace element (WHO)

Step 1: estimation of the physiological requirement ($R_{phys}$)
→ measuring the daily losses

Step 2: estimation of the minimum requirement ($R_{min}$)
→ taking the average bioavailability into account:

$$R_{phys} \times 100 / \text{bioavailability} (%)$$

Step 3: Deriving dietary reference values (+ safety margin):
Determination of the usual intakes that would meet the condition that only few people are below their own requirement (97th percentile) → CV + (15 % x 2)
### Estimated bioavailability of minerals and trace elements in humans

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Bioavailability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>20 - 40 %</td>
</tr>
<tr>
<td>Magnesium</td>
<td>20 - 30 %</td>
</tr>
<tr>
<td>Zinc</td>
<td>10 - 90 % (~30 %)</td>
</tr>
<tr>
<td>Copper</td>
<td>35 - 70 %</td>
</tr>
<tr>
<td>Iron</td>
<td>10 - 25 % (5-8 % plant)</td>
</tr>
<tr>
<td>Chromium</td>
<td>1 - 10 % (~ 2 %)</td>
</tr>
<tr>
<td>Selenium</td>
<td>50 - 95 %</td>
</tr>
<tr>
<td>Iodine</td>
<td>50 - 95 %</td>
</tr>
</tbody>
</table>
Deriving dietary reference values

Healthy people:

minimum requirement
+ safety margin

Dietary Reference Values

People with special physiological conditions:

minimum requirement
+ extra requirement
+ safety margin

Dietary Reference Values
Deriving dietary reference values for specific conditions

**Extra requirement** in specific conditions:

- growth
- pregnancy
- lactation
- intensive physical activities or hot/humid climate (→ nutrient loss through sweat)
- certain diseases
- old age (?)
Zinc absorption from diet

- Absorption in duodenum by an active mechanism
- Absorption rate \( \sim 30\% \) from a moderate availability diet (dependent to supply status!)
- Balance studies: reduced absorption with aging
  - 20-30 y.: \( 31 - 39\% \)
  - 65-74 y.: \( 17 - 21\% \)
- Interactions: high intake of iron or copper
  \( \rightarrow \) can interfere with and reduce zinc absorption
- Elimination: mostly via feces; less via urine
Calculation of the DRV for zinc (adults)

Physiological requirement:  
- m: 2.2 mg/day  
- w: 1.6 mg/day

Bioavailability:  
~ 30 %

Minimum requirement:  
- m: 7.5 mg/day  
- w: 5.5 mg/day

DRV (15 % CV \(\rightarrow\) + 30 %)  
- m: = 10 mg/day  
- w: = 7 mg/day
Zinc sources from food

- Meat, fish, shellfish, offals (liver), cheese, milk, eggs, cereal (whole wheat) and legumes are the main sources of zinc intake.
- Bioavailability of zinc from foods of animal origin is much better than from plant foods.
Factors influencing the bioavailability of zinc

- Absorption promoting factors:
  -> proteins, peptides, amino acids

- Absorption inhibiting factors:
  -> phytate (e.g. in cereals), high iron or copper intake, high intake of calcium, phosphate and heavy metal)
<table>
<thead>
<tr>
<th>Food</th>
<th>Zinc Content [mg/100g]</th>
</tr>
</thead>
<tbody>
<tr>
<td>oysters</td>
<td>6 – 160</td>
</tr>
<tr>
<td>beef</td>
<td>4,3</td>
</tr>
<tr>
<td>gouda cheese</td>
<td>3,9</td>
</tr>
<tr>
<td>wheat (whole-corn)</td>
<td>2,7</td>
</tr>
<tr>
<td>pork</td>
<td>2,0</td>
</tr>
<tr>
<td>eggs</td>
<td>1,4</td>
</tr>
<tr>
<td>chicken</td>
<td>1,0</td>
</tr>
<tr>
<td>wheat flour (Type 405)</td>
<td>1,0</td>
</tr>
<tr>
<td>milk</td>
<td>0,4</td>
</tr>
</tbody>
</table>
# Absorption rate of zinc from food

<table>
<thead>
<tr>
<th>Food</th>
<th>Absorption Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>wheat bran</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>whole wheat bread</td>
<td>11%</td>
</tr>
<tr>
<td>beef</td>
<td>20%</td>
</tr>
<tr>
<td>turkey</td>
<td>30%</td>
</tr>
<tr>
<td>cornflakes with milk</td>
<td>36%</td>
</tr>
<tr>
<td>chicken</td>
<td>37%</td>
</tr>
</tbody>
</table>
Zinc absorption by humans from aqueous solutions of zinc (●) or from single meals from which zinc is moderately available (▲) (WHO, 1996)
Factors influencing the bioavailability of iron

- **Absorption promoting factors:**
  - ascorbic acid, meat proteins

- **Absorption inhibiting factors:**
  - phytate (eg in cereals), high zinc or copper intake, high intake, phosphate and oxalic acid
Iron: main sources

- Bread, meat, sausages, vegetables and legumes as the main sources for the supply of iron
- Body can utilize iron from foods of animal origin such as better from plant foods
Important iron sources

- 25.7% bread and bakery goods
- 22.3% meat, meat products and sausages
- 9.4% vegetables and vegetable products
- 8.7% beverages
- 6.3% pasta and others
- 5.5% eggs
- 5.2% potatoes
- 4.3% fruits, fruit products
- 2.4% milk, milk products
Absorption rate of iron from food (1)

Food from plant origin:

- rice 1 %
- spinach 1 – 1.5 %
- corn 3 %
- lettuce 4 – 5 %
- wheat 5 %
- soy beans 5.5 %
Absorption rate of iron from food (2)

Food from animal origin:

- ferritin: 5 – 6%
- liver: 10 – 18%
- fish: 10 – 12%
- hemoglobin: 12 – 15%
- meat: 20 – 25%
Calculation of the DRV for iron (adult)

Minimum requirement:  
m: 1,0 mg/day  
w: 1,5 mg/day

Bioavailability: mixed diet  
5-15 mg non heme-iron/day  
1-5 mg heme-iron/day

DRV  
m: = 10 mg/day  
w: = 15 mg/day
<table>
<thead>
<tr>
<th>Alter</th>
<th>Eisen</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/Tag</td>
<td>mg/MJ¹ (Nährstoffdichte)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>m</td>
<td>w²</td>
<td>m</td>
</tr>
<tr>
<td><strong>Säuglinge³</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 bis unter 4 Monate⁴,⁵</td>
<td>0,5</td>
<td>0,3</td>
<td>0,3</td>
</tr>
<tr>
<td>4 bis unter 12 Monate</td>
<td>8</td>
<td>2,7</td>
<td>2,8</td>
</tr>
<tr>
<td><strong>Kinder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 bis unter 4 Jahre</td>
<td>8</td>
<td>1,7</td>
<td>1,8</td>
</tr>
<tr>
<td>4 bis unter 7 Jahre</td>
<td>8</td>
<td>1,3</td>
<td>1,4</td>
</tr>
<tr>
<td>7 bis unter 10 Jahre</td>
<td>10</td>
<td>1,3</td>
<td>1,4</td>
</tr>
<tr>
<td>10 bis unter 13 Jahre</td>
<td>12</td>
<td>1,3</td>
<td>1,8</td>
</tr>
<tr>
<td>13 bis unter 15 Jahre</td>
<td>12</td>
<td>1,1</td>
<td>1,6</td>
</tr>
<tr>
<td><strong>Jugendliche und Erwachsene</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 bis unter 19 Jahre</td>
<td>12</td>
<td>1,1</td>
<td>1,8</td>
</tr>
<tr>
<td>19 bis unter 25 Jahre</td>
<td>10</td>
<td>0,9</td>
<td>1,9</td>
</tr>
<tr>
<td>25 bis unter 51 Jahre</td>
<td>10</td>
<td>1,0</td>
<td>1,9</td>
</tr>
<tr>
<td>51 bis unter 65 Jahre</td>
<td>10</td>
<td>1,1</td>
<td>1,4</td>
</tr>
<tr>
<td>65 Jahre und älter</td>
<td>10</td>
<td>1,2</td>
<td>1,4</td>
</tr>
<tr>
<td><strong>Schwangere</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>3,3</td>
<td></td>
</tr>
<tr>
<td><strong>Stillende⁶</strong></td>
<td>20</td>
<td>1,9</td>
<td></td>
</tr>
</tbody>
</table>

¹ Berechnet für Jugendliche und Erwachsene mit überwiegend sitzender Tätigkeit (PAL-Wert 1,4)
² Nichtmenstruierende Frauen, die nicht schwanger sind oder nicht stillen: 10 mg/Tag
³ Ausgenommen Unreifgeborene
⁴ Hierbei handelt es sich um einen Schätzwert
⁵ Ein Eisenbedarf besteht infolge der dem Neugeborenen von der Plazenta als Hb-Eisen mitgegebenen Eisenmenge erst ab dem 4. Monat
⁶ Diese Angabe gilt für stillende und nicht stillende Frauen nach der Geburt zum Ausgleich der Verluste während der Schwangerschaft
Trace element supply situation in Germany

- Trace element supply of consumers is primarily dependent on the bioavailability and less on the absolute amount of intake.
- Due to the high consumption of foods of animal origin overall a good supply with trace elements is observed.
- Exception: iodine