Meat as a healthy and valuable source of micronutrients

Abstract
During the last decades meat and especially liver have been looked upon as unhealthy food with high fat content and carcinogenic potential. In addition, its content of highly valuable micronutrients has mostly been ignored. As a result, the mean uptake and serum levels of several micronutrients in the population are below the recommended levels. In the meantime, the contamination of liver with heavy metals and other contaminants has fallen far below the allowed thresholds and sometimes even below the detection limit while levels of several micronutrients in the population are below the recommended levels. In the meantime, the contamination of liver with heavy metals and other contaminants has fallen far below the allowed thresholds and sometimes even below the detection limit while levels of several micronutrients in the population are below the recommended levels.

Keywords
Micronutrients, meat, liver, human nutrition, human health

Introduction
Many people consider meat, especially red meat, as unhealthy food, mainly due to its postulated "high" fat content and its very recently posted "reputation" that red meat is a promoter of colon cancer. As a consequence, low or no meat intake is often recommended to avoid or minimize the risk of cancer, obesity and metabolic syndrome. Ethical arguments against intensive animal farming and its impact on global climate change contribute to the negative image of meat, but will not be addressed in this review.

These more or less justified arguments against meat consumption ignore the fact that meat is a valuable source for some essential micronutrients such as iron, selenium, vitamins A, B12 and folate. Some of these are not present in plants at all or have such a low bioavailability that eating only plant-derived food may be inadequate to meet the daily requirement. The fact that the world wide inadequacy of some micronutrients ("hidden hunger") is related primarily to iron, zinc, vitamin A and folate is a result of rather poor diet diversity with the major component being starchy food and with a very low supply of meat and meat derived products (Besalski 2016). Meat is an important food as an essential part of a mixed diet that ensures adequate delivery of micronutrients and amino acids even in low amounts. If meat and meat derived products are completely avoided the risks of inadequate supply and subsequent health relevant negative effects (increased infectious diseases, impairment of the immune system, anemia etc.) may occur.

Meat as an important source of micronutrients
Vitamin A and vitamin B12 occur only in meat and can hardly be compensated for by plant-derived provitaminas: a provitamin (B12 does not exist and provitamin A, ß-carotene, would have to be taken up in highest amounts to meet the daily vitamin A recommendation (1 mg) due to its poor conversion rate of 1:12 (0.2 mg provitamin A needed to achieve 1 mg Vitamin A).

Iron has a higher bioavailability when derived from meat as hem iron than plant-derived non-hem iron. Similarly, folic acid from meat (especially liver) and eggs has a nearly ten-fold higher bioavailability than from vegetables. Consequently low or no intake of meat (including liver) poses a risk for inadequate supply and symptoms of deficiency. Meat is also an excellent source for Thiamine (B1) and Riboflavin (B2). These nutrition facts lead to the question whether people with "normal" eating habits or only special groups of people are at risk for deficiencies of meat-derived micronutrients.

One risk group are elderly people who are generally considered at risk to develop vitamin and trace element deficiencies, especially for the vitamins A, D, E, and folate as well as iron and calcium (Anderson 2001; Bates et al. 2002; Martins et al. 2002; Viteri and Gonzalez 2002). Recently a meta-analysis summarized the data from 41 studies with community-dwelling older adults (Ter Borg et al. 2015). 30 % were below the Estimated Average Requirement (EAR), for Vitamin A, 95 % for vitamin D, 40 % for folate, vitamin B1 and B2 and 15 % for iron. Per definition 50 % below the EAR and 50 % above the EAR are not at risk for deficiency. Adding two standard deviations to the EAR is used to calculate the reference value. Consequently, according to the definition of the EAR a supply below results in an increasing risk for developing a deficiency with clinical consequences. Malnutrition is far more common among institutionalized and chronic hospitalized elderly compared to free-living subjects in the community and the prevalence of malnutrition is associated with the severity of morbidity, functional impairments and mental state. Thiamine and folate status need special attention in this respect, as a deficiency of these nutrients is associated with depression and impaired cognition and dementia. Indeed, supplementation with folic and vitamin B12 resulted in a significant positive impact on mood and cognitive vigilance (von Arnim et al. 2013).

Pregnant women are another group at risk for micronutrient deficiencies. Their adequate nutrition plays an important role in the well-being of mother and child and also influences the health of the offspring not only during its intrauterine life but also during childhood and adolescence (intra-uterine or prenatal programming). While the enhanced requirements during pregnancy are met by a balanced diet and physiological adaptive processes, the micronutrient status of vitamin A, D, folic acid, iron, and zinc may become compromised without supplementation (Opper et al. 1993; Fögelsröm 1999; Salehi et al. 2008) especially when meat is avoided, which can be frequently seen in women in the child bearing age.

Selected micronutrients from meat and liver
Meat and liver are excellent sources for a number of micronutrients. Low-fat pork contains 1.8 mg iron and 2.6 mg zinc; pig liver contains 360 mg magnesium, 20 mg iron and 60 mg selenium per 100 g. Thus, meat and liver (100g/day) can cover up to 50 % of the Recommended Daily Allowance (RDA) for iron, zinc, selenium, vitamins B1, B2, B6, and 100 % of vitamin A.

Another reason to include liver in the diet is that newest results show porcine as well as bovine liver to be almost free of harmful substances like heavy metals (a former reason to avoid the uptake of liver) which are far below the allowed thresholds or even below the technical detection limit (DGE 2004).

Vitamin A
The best source for vitamin A is liver. Liver of pork and beef contains 6.0 μg and 20 μg of vitamin A respectively (tab 1). However, liver consumption is low and restricted to some areas in Germany where it is a traditional food. The argument that liver should be avoided in a healthy diet has been based primarily on suspected contaminants in the liver (e.g. hormones, xenobiotics, metals etc.) which nowadays are seldom detected (see above). ß-carotene from vegetables were the only source of vitamin A, more than 500 g mixed and liver carpito rich vegetables per day must be consumed to reach the recommended 1 mg retinol. This amount of vegetables...
Table 1: Selected mineral and vitamin contents in different animal products

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Pork</th>
<th>Beef</th>
<th>Broiler breast</th>
<th>Turkey breast</th>
<th>Duck</th>
<th>Pork</th>
<th>Beef</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca (mg)</td>
<td>5.1</td>
<td>5.7</td>
<td>15.0</td>
<td>25.0</td>
<td>11.0</td>
<td>7.6</td>
<td>5.8</td>
</tr>
<tr>
<td>Mg (mg)</td>
<td>26</td>
<td>23</td>
<td>29.0</td>
<td>24.0</td>
<td>16.0</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>Fe (mg)</td>
<td>1.0</td>
<td>2.1</td>
<td>1.0</td>
<td>1.9</td>
<td>2.7</td>
<td>17</td>
<td>6.9</td>
</tr>
<tr>
<td>Zn (mg)</td>
<td>2.4</td>
<td>4.3</td>
<td>1.0</td>
<td>2.9</td>
<td>1.9</td>
<td>6.5</td>
<td>4.8</td>
</tr>
<tr>
<td>Se (µg)</td>
<td>12</td>
<td>5.4</td>
<td>27.6</td>
<td>37.2</td>
<td>20.0</td>
<td>56</td>
<td>21</td>
</tr>
<tr>
<td>Vit C (mg)</td>
<td>ND</td>
<td>ND</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td>Vit A (µg)</td>
<td>6.0</td>
<td>20</td>
<td>21</td>
<td>0</td>
<td>63</td>
<td>36</td>
<td>1000</td>
</tr>
<tr>
<td>Vit D (µg)</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>1.7</td>
</tr>
<tr>
<td>Vit E (µg)</td>
<td>410</td>
<td>480</td>
<td>300</td>
<td>300</td>
<td>700</td>
<td>60</td>
<td>746</td>
</tr>
<tr>
<td>Folate (µg)</td>
<td>2.5</td>
<td>3.0</td>
<td>4.0</td>
<td>7.0</td>
<td>6.0</td>
<td>136</td>
<td>592</td>
</tr>
<tr>
<td>B1(mg)</td>
<td>0.9</td>
<td>0.057</td>
<td>0.1</td>
<td>0.1</td>
<td>0.2</td>
<td>0.31</td>
<td>0.02</td>
</tr>
<tr>
<td>B2(mg)</td>
<td>0.23</td>
<td>0.26</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>3.2</td>
<td>3.1</td>
</tr>
<tr>
<td>B6(mg)</td>
<td>0.575</td>
<td>0.24</td>
<td>0.6</td>
<td>0.4</td>
<td>0.2</td>
<td>0.59</td>
<td>0.96</td>
</tr>
<tr>
<td>B12(µg)</td>
<td>2.0</td>
<td>5.0</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>39</td>
<td>65</td>
</tr>
</tbody>
</table>

1 Souci-Fachmann Kraut | www.nutritiondata.self.com

Vitamin B12

Vitamin B12 is found only in animal products. In a recent UK study of 250 vegetarians and 250 vegan men, approximately one quarter of vegetarians and more than half of vegans had sub-optimal intakes of vitamin B12. Plasma vitamin B12 levels were low in the vegetarians and extremely low in the vegan group, with more than a quarter below the threshold level where neurological signs may develop (Dror and Allen 2008; Gilsing et al. 2010). Elderly non-vegetarian people are also at risk of vitamin B12 deficiency, due to physiological changes resulting in reduced absorption. In the UK, vitamin B12 status in some people aged 65 and over was inadequate. Therefore, vitamin B12 intake was adequate when compared with UK dietary reference values (Finch et al. 1998). To assure the RDA of vitamin B12 (3 µg/day for adults), again meat (bovine 5 µg/100 g) and especially liver (depending on the species) are the best sources.

Iron

Although iron is one of the most abundant elements in the Earth’s crust, iron deficiency is the most common and widespread nutritional disorder in the world. According to the WHO (2008), iron deficiency adversely affects the cognitive performance, behaviour, and physical growth of infants, pre-school and school-aged children; the immune status and morbidity from infections of all age groups; the use of energy sources by muscles and thus the physical capacity and work performance of adolescents and adults of all age groups.

The iron concentration in meat is between 1-3 mg/100g. Liver contains between 8 mg/100 g (calf) and 16 mg/100 g (pig). In bread and legumes, the concentration varies between 1 mg up to 8 mg/100 g. Due to biological loss, such as cyclical monthly bleeding of fertile-aged women, may actually contain more contaminants than a portion of liver, as their concentration in vegetables and fruits seem to have increased during the late 1990th and early 2000th (De Bree et al. 2004). A small portion of liver (100 g) twice a month supplies sufficient vitamin A and is neither toxic nor teratogenic. A poor vitamin A-status which cannot be easily detected via blood analysis due to its homoeostatic regulation increases the risk for respiratory tract diseases and impairment of the immune system (Bresalski 2013).

Folate

In European countries the average folate intake in adults was found to be remarkably similar, around 380 µg/day in adult men and 250 µg/day in adult women (De Bree et al. 1997). This is below the former recommended intake level of 400 µg/day (which has recently been reduced to 300 µg/day) and too low for pregnant women and women planning a pregnancy. For these groups an intake of 600 µg/day is considered protective against Neural Tube Defects (NTD), which appears in around 700 cases/year in Germany. More than 90 % of women of child-bearing age have sub-optimal dietary folate intake. Supplementation of folate to the optimal level can reduce the risk to develop NTD by up to 70 %. Data regarding meat derived folate intake and NTD is not available. It should be considered that meat and liver in particular are sources with better bioavailability than plant derived folate.

Due to the fact that females in child bearing age are not adequately supplied with folate, supplements (400 µg/day) are strongly recommended.

Table 2: Hazard ratio of red meat, processed meat and poultry consumption (observed and calibrated by 1-hour recall data)² for all-cause mortality

<table>
<thead>
<tr>
<th>Source</th>
<th>Observed HR</th>
<th>Calibrated HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red meat (per 100 g)</td>
<td>1.02 (0.98–1.06)</td>
<td>1.02 (0.98–1.06)</td>
</tr>
<tr>
<td>Processed meat (per 50 g)</td>
<td>1.09 (1.06–1.12)</td>
<td>1.18 (1.11–1.25)</td>
</tr>
<tr>
<td>Poultry (per 50g)</td>
<td>0.96 (0.92–0.99)</td>
<td>0.95 (0.85–1.04)</td>
</tr>
</tbody>
</table>

² A 24-hour dietary recall (24HR) is a structured interview intended to capture detailed information about all foods and beverages, consumed by the respondent in the past 24 hours. This method was used to provide more reliable data on consumption. https://dietassessmentprimer.cancer.gov/profiles/recall/
excessive infestation with blood-feeding parasites, or poor bioavailability of iron from plant-based diets, it is estimated that as many as 3.4 billion people, around 20%, in high-income and 50-60% in low-income countries may have inadequate iron supply with the diet. At any given time, 1.62 billion people – over 30% of the world’s population – are anemic, mainly due to iron deficiency. In developing countries this is frequently exacerbated by malaria and worm infections (WHO, 2008). The highest prevalence (47-4%) has been found in preschool children and non-pregnant females.

In a recent Irish food consumption survey, almost half of women aged 18-50 year had inadequate iron intakes when compared with national average requirements. Around 25% of all pregnant women in Europe suffer from iron deficiency. The daily supply is below 60 % of the estimated average requirement (EAR) for pregnancy (Blumfeld et al., 2015). Breastmilk is low in iron, in particular when the supply of the mother is inadequate. In a recent study in Germany 21 % of breast fed children were iron deficient and 6% had clear symptoms of anemia (Xuβ et al. 2010). During postweaning age (12 - 23 months) 15 % of male and 18.5 % of female children in Germany had an inadequate supply (below EAR) (Hitger et al., 2015). In the British National Diet and Nutrition Survey, iron intake was found to be low in girls (aged 7-18 years) and decreased with age. Adolescent females (15-18 year) were found to have extremely low intakes of iron when compared to UK dietary reference values.

Depending on the composition of the individual diet the bioavailability of iron can differ 5 to 10-fold. The bioavailability depends on the presence or absence of different ligands (phytate and other cereals, products, tannins from coffee and tea and oxalates from vegetables) which form complexes with iron and zinc and block their absorption. Diets primarily composed of vegetables, rice, beans and corn are associated with poor iron bioavailability. This explains the high incidence of anemia in developing countries. 100 g pork meat and an even lower amount of liver added to a vegetarian diet increases the iron absorption 3.6 fold.

Zinc
Zinc is essential for more than 100 enzymes and plays an important role within the immune system. Zinc deficient individuals demonstrate slower wound healing and are more prone to infections. Some studies showed that zinc may beneficially affect cold symptoms; however a meta-analysis of randomized controlled trials concluded that there is no evidence for the effectiveness of supplemental zinc in reducing the duration of common cold symptoms (Jackson et al. 2000). Especially in elderly a reduced zinc status is evident (Liukkio et al. 2004). In the same group, a higher protein intake (together with slight exercise) stopped sarcopenia, a progressive loss of lean body mass. The RDA for zinc is about 12-15 mg/day. A higher need of zinc is documented (20-25 mg/day) during pregnancy and lactation as well as during chronic inflammatory diseases (Rink and Gabriel, 2000).

Meat contains between 2 and 10 mg of zinc/100g Plant derived food is also a good source, in particular green leafy vegetables (up to 70 mg/1000 kcal) but due to the more reliable bioavailability meat seems a safer source of zinc.

Considering the nutrition value of vegetarian diets, beside vitamin B12, iron and zinc are the micronutrients of greatest concern.

Bioavailability of iron and zinc is substantially decreased through the interaction with phytate and further constituents of plant food.

Meat and cancer
Meat consumption, especially red meat, is not carcinogenic per se, even if it contains components which are assumed to contribute to cancer formation. On the other hand, persons with a high intake of fruits and vegetables are considered to have a reduced cancer risk because of protecting factors such as carotenoids, flavonoids, further phytochemicals and also folic acid, selenium, zinc and other components. It is not clear why these latter compounds should be less effective if they reach the body via meat. The balance of promoting and protecting factors within the diet is important for the protection against cancer. Furthermore, the insulin-resistance hypothesis shows that a nutritional behavior leading to a metabolic syndrome (high energy, high glycaemic carbohydrates) might favor colon cancer or even other types of cancer. The “goals for nutrition in the year 2000” (Willett, 1999) give a very good and comprehensive advice: “Current nutritional recommendations for the prevention of cancer include increased consumption of fruits and vegetables; reduced consumption of red meat and animal fat; and avoidance of excessive alcohol”.

Very recently the WHO classified red meat as class 2A carcinogenic based on epidemiological data. Class 2A means that there is sufficient evidence of carcinogenicity in humans. However the data used are based on limited evidence from epidemiological studies. Limited evidence describes a result which shows an association between exposure of red meat and cancer but other reasons for the increased risk cannot be excluded. This limited evidence is a conclusion in all meta-analysis dealing with red meat intake and cancer risk (Alex- ander et al. 2015, Eggberg et al. 2015, Lipp et al. 2015, Pham et al. 2014). Different epidemiological studies between 2000 and 2013 were used to justify the relation between high meat intake and increased risk for Colorectal Cancer (CRC) as the basis for the cancer risk classification. The European Prospective Investigation into Cancer and Nutrition (EPIC) study, a big human cohort study with more than 500,000 participants showed that the highest daily intake of meat (160 g/day) has a relative risk of 1.35 compared to the lowest intake (Norat et al. 2005). Red meat alone (> 80 g/day) increased the risk 1.17 %, processed meat (>80 g/day) increased the risk up to 1.42 %. A meta-analysis (Chan et al. 2011) with 10 cohort studies documented a relative risk for the highest intake (140 g/day) of 1.14 % compared to the lowest. Further increase of meat consumption did not change the relative risk. Based on that study the International Agency for Research on Cancer (IARC) distributed the warning and the risk classification (Bouwad et al. 2015). A more detailed examination of the EPIC cohort, however, showed a more differentiated result:

Depending on the model used (uncalibrated or calibrated), only processed meat showed a risk increase of 50 g additional meat/day. The impact of daily processed meat consumption on the risk to develop cancer shows a U-shaped pattern. The lowest consumption of processed meat has the same mortality as a daily intake of approx. 55 g.

In contrast, red meat consumption in the highest quartile vs. lowest did not show a significant increase in cancer mortality. There was no association between intake of poultry and all-cause mortality.

A very recent meta-analysis with 27 prospective studies and a broader evaluation of the relative risk estimates by specific intake levels documented again a rather weak relation between red meat consumption and CRC risk (Figure 2).

At intake levels > 100 g red meat per day showed a slightly increased risk (1.20 %). The elevation of the relative risk related to servings per day is largely influenced by male participants. Alexander et al. (2015) concluded:

“In the current meta-analysis of red meat intake and CRC (colorectal cancer), we comprehensively examined associations...”

Figure 2: Dose response patterns showing the relative risk to develop Colorectal Cancer (CRC) based on meta-analyses of categorical intake groupings (adapted from Alexander et al. 2015)
by creating numerous subgroup stratifications, conducting extensive sensitivity ana-
lysies, and evaluating dose-response using several different methods. Associations
between red meat and CRC were weak to nonexistent. Of the highest categories of
intake in the individual studies, over one-
third of the RRs (relative risks) were 1.0 or lower, and almost half were less than 1.05.
Summary associations were weak, with most SRREs (summary relative risk estima-
tes) around the null value or just slightly above. Because of multiple comparisons
(i.e., over 70 separate analyses were con-
ducted), some statistically significant corre-
lations could arise by chance alone.

In conclusion, based on the quantitative
findings and scientific rationale for inter-
pretation documented in the current meta-
analytic, red meat intake does not appear
to be an independent predictor of CRC risk.

The relation between slight but insigni-
ficant risk increase and servings per day shows that the best way to be on the safe
side with respect to either cancer risk or in-
adquate micronutrient intake is a mixed and balanced diet. Indeed, a simple and
very old suggestion.

Conclusions
Any kind of an unbalanced diet, either avoiding meat or fruit or vegetables may lead to (micro-) nutrient deficiencies and consecutive disorders especially in groups with higher needs (pregnant or lactating
women, elderly, etc.). At this time one has to
assume, that a mixed and balanced diet
would be recommended, actual and desired intake.


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