

Review

Meat as a component of a healthy diet – are there any risks or benefits if meat is avoided in the diet?

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Received 30 June 2004; received in revised form 15 July 2004; accepted 15 July 2004

Abstract

Meat is frequently associated with a “negative” health image due to its “high” fat content and in the case of red meat is seen as a cancer-promoting food. Therefore, a low meat intake, especially red meat is recommended to avoid the risk of cancer, obesity and metabolic syndrome. However, this discussion overlooks the fact, that meat is an important source for some of micronutrients such as iron, selenium, vitamins A, B12 and folic acid. These micronutrients are either not present in plant derived food or have poor bioavailability. In addition, meat as a protein rich and carbohydrate “low” product contributes to a low glycemic index which is assumed to be “beneficial” with respect to overweight, the development of diabetes and cancer (insulin resistance hypothesis). Taken together meat is an important nutrient for human health and development. As an essential part of a mixed diet, meat ensures adequate delivery of essential micronutrients and amino acids and is involved in regulatory processes of energy metabolism.

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Keywords: Meat; Processed meats; Nutrition; Fat; Proteins; Micronutrients; Cancer; Protecting factors

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1. Introduction

Meat is frequently associated with a “negative” health image due to its “high” fat content and in the case of red meat is seen as a cancer-promoting food. Therefore a low meat intake, especially red meat is recommended to avoid the risk of cancer, obesity and metabolic syndrome. However, this discussion overlooks the fact, that meat is an important source for some micronutrients such as iron, selenium, vitamins A, B12 and Folic acid. These micronutrients are either not present in plant derived food or have a poor bio-availability. In addition, meat as a protein rich and carbohydrate “low” product contributes to a low glycemic index which is assumed to be “beneficial” with respect to obesity, diabetes development and cancer (insulin resistance hypothesis). Taken together meat is an important nutrient for human health and development. As an essential part of a mixed diet, meat ensures adequate delivery of essential micronutrients and amino acids and is involved in regulatory processes of energy metabolism. The following article will review the role of meat as a source of micronutrients, especially for groups at risk for low intake or higher need and the importance of the single micronutrients for maintaining health.

Is there any benefit, if meat is avoided in human nutrition? Does meat promote or prevent cancer? It is frequently argued that a diet which contains only “traces” of meat or excludes meat completely might prevent colon cancer. Based on a couple of studies and with respect to the cancer preventive effects of selected nutrients present in meat, this hypothesis seems more and more unlikely.

2. Proteins

It has been assumed, based on per capita protein intake and colon cancer risk, that total protein, is related to colon cancer risk (Youngman & Cambell, 1998). However, the majority of epidemiological cohort and case control studies could not confirm these assump-

tions. Only for red meat derived protein is there some evidence that risk increases if red meat is consumed twice a day and more (MacIntosh & Le Leu, 2001) or processed (boiled or fried). Whether the non-fat matrix of meat, e.g., the amino acid composition or the amount of heme iron plays a role in carcinogenesis is not understood. McIntosh and coworkers observed a non-significant increase from 33% to 59% in the incidence of DMH-induced (differential methylation hybridization) intestinal tumours in mature rats when barbecued beef was substituted for whey protein concentrate against a high fat (20%) diet background (MacIntosh, Royle, & Le Leu, 1998). Whether the concentration of protein in a diet determines the risk for cancer is controversial (MacIntosh, & Le Leu, 2001). In contrast the type of protein seems more important with respect to carcinogenesis. A high methionine diet, determined by type of protein as well as quantity ingested, has been reported to lead to increased circulating insulin which has been assumed to contribute to colon carcinogenesis (McKeown-Eyssen, 1994). From epidemiological studies there is accumulating evidence that support the insulin resistance (IR) hypothesis to explain the risk from colon cancer. It was hypothesised that IR leads to increased initiation and promotion of colon cancer by elevating serum insulin as a growth factor or raised glucose and triglycerides as fuels (McKeown-Eyssen, 1994). Bruce, Wolever, and Giacca (2000) summarise different reasons which strengthen the hypothesis: colon cancer patients frequently have evidence of glucose intolerance and insulin resistance (IR); cohorts of type 2 diabetes have been found to have an excess mortality due to colon cancer; cohort and case control studies have revealed a clear association of early colon cancer, colon cancer and colonic polyps with increased levels of fasting insulin, triglycerides, VLDL (very low density lipoproteins) and abdominal obesity; subjects who developed colonic polyps consumed more carbohydrates with a higher glycemic index than controls; recent case control studies have also shown an association between plasma insulin like growth factor I (IGF-I), which is often increased in insulin resistant individuals, and IGF-binding protein (IGF-BP) levels with risk for colon cancer. From a

couple of animal experiments there is evidence that IR leads to an increased colon cancer risk.

Diets with a high glycemic index are thought to be associated with or to favour insulin resistance (Frost, Leeds, & Trew, 1998). Red meat, however, has a low glycemic index and may not contribute to the metabolic syndrome as long as its fat/energy content does not contribute primarily to the daily energy intake. Koohestani, Tran, and Lee (1997) showed that a high fat diet promotes aberrant crypt formation (ACF) in IR rats as an important step in colon carcinogenesis. Based on their results they conclude that: diets high in energy, saturated fat, and glycemic carbohydrate and low in ω 3-fatty acids could deleteriously affect cell signalling in colonic cells in ways that lead to IR and colon cancer. Dietary intervention that reduces IR may also reduce colon cancer risk. So far low fat meat seems not to contribute to colon cancer.

3. Fat

Several epidemiological early case control and cohort studies suggested a positive correlation between fat intake and incidences of breast-, colon- and prostate cancer (Potter, Slaterry, & Bostick, 1993; Schottenfeld & Fraumeni, 1996). However, more recent cohort, large case control and pooled analysis of 13 case control studies failed to detect an association between fat intake and colon cancer (Giovannucci, Rimm, & Stampfer, 1994; Howe, Aronson, & Benito, 1997). The relation between dietary fat intake and breast cancer has been examined in a couple of prospective studies. In a pooled analysis no overall association was seen for total fat intake over the range of 15% to > 45% of energy from fat (Hunter, Spiegelman, & Adami, 1996). In contrast, among the small number of women consuming less than 15% of energy from fat, breast cancer risk was elevated twofold. With respect to prostate cancer, the few existing studies show a relative consistency in supporting an association between consumption of fat-containing animal products and cancer incidence. However, the majority of the studies were not adjusted for total energy intake. Studies adjusting for energy intake did not find an increased risk (Kolonel, 2001). Meat intake however, correlates more or less with prostate cancer risk. Sixteen out of 22 case control or cohort studies showed an increased risk above a risk ratio of 1.3. A recent prospective study (Michaud, Augustsson, & Rimm, 2001) documented an elevated risk (RR, relative risk) of prostate cancer (RR 1.47) from red meat consumption (>5/week). Up to 2–4 times a week the RR was below 1.0 (0.96) demonstrating that moderate red meat consumption as usually recommended does not contribute to prostate cancer risk.

In spite the long history of studies on fat and cancer, there remains some controversy. It is more or less generally suggested that animal fat rich in saturated fat is more closely related to cancerogenesis and plant-derived mostly unsaturated fat (PUFA) is more protective. In animal models, the tumour promoting effect of fat intake has been observed primarily for PUFA (Hopkins & Carroll, 1979; Hopkins, Kennedy, & Carroll, 1981). A couple of studies show that polyunsaturated ω 6 fatty acids (linoleic acid) enhance cancer development in rodents (Carroll, 1991; Fay, Freedman, & Clifford, 1997). The prostaglandin E2 (PGE2) seems to be involved in colon carcinogenesis and is formed from ω 6 fatty acids (arachidonic acid). EP1 (PGE2-receptor) k.o. mice showed resistance to AOM induction of neoplastic colon lesions (Watanabe, Kawamori, & Natatsugi, 1999). ω 3 fatty acids (linolenic acid) however, suppress colon carcinogenesis by inhibiting the arachidonic pathway (Takahashi, Fukutake, & Isoi, 1997).

The suggestion that consumption of red meat as a source of dietary fat increases risk of colon cancer is based on the rather simple fat-colon cancer hypothesis, which is based on the premise that dietary fat promotes excretion of bile acids which can be converted to carcinogens (Reddy, 1981). The controversial results from different studies and the fact that meta analyses show that fat might have a rather minor role, if even any, in cancerogenesis of the colon or in other cancer sites might be explained in different ways. The fat content of red meat varies in a wide range and shows different patterns. Palmitic acid but not stearic acid present in different amounts in red meat has been shown to be a strong mitogen of adenoma cells in culture (Friedman, Isaksson, & Rafter, 1989). Fat, derived from red meat, might be less absorbed, due to either its composition (stearic acid) or due to matrix (muscle) interactions. Polymorphisms of genes involved in the expression of cleavage and re-esterification of triglycerides may also play important roles regarding individual susceptibility. Finally, components not belonging to lipids might contribute to carcinogenesis such as HCAs (heterocyclic amines) or at least the iron content of meat. Dietary iron enhances lipid peroxidation in the mouse colon (Younes, Trepkau, & Siegers, 1990) and increases the incidence of DMH-induced colorectal tumours in mice and rats (Nelson, Yoo, & Tanure, 1989; Siegers, Bumann, Baretton, & Younes, 1988). Indeed, studies in humans point on a relationship between body iron stores and the incidence of colon tumours (Knekt, Reunanen, & Takkunen, 1994a; Stevens, Jones, & Micozzi, 1988). Finally carcinogens and promoters, e.g., HCAs are formed when meat is fried or cooked and may contribute more or less to the individual cancer risk, especially in colorectal, breast and prostate cancer.

4. Processed meat and genetic polymorphisms

HCAs are converted to their hydroxyamino derivatives by cytochrome P450s especially CYP 1A2 and further activated by esterification enzymes acetyltransferase and sulfotransferase. The reactive ultimate forms produce DNA adducts with guanines at their C8 position, resulting in base substitution and at least mutation. Similarly, oxidative modification of the DNA via reactive oxygen species (ROS) results in the formation of 8-oxo-deoxy-guanin with subsequent base substitution and mutation.

Epidemiological studies revealed some positive (Zheng, Gustaffson, & Sinha, 1998) and some negative (Augustsson, Skog, Jägerstad, Dickman, & Steineck, 1999) links between cancer risk and intake of well-done meat or fish. Studies that have examined intensity of cooking have tended to show positive associations with breast cancer (Knekt, Steineck, & Järvinen, 1994b), others not (Ambrosone, Freudenheim, & Sinha, 1998). The latter investigated the role of genetic polymorphisms of enzymes involved in DNA adduct formation of HCAs, which could play at least a critical role in individual cancer susceptibility. HCAs require enzymatic activation to bind to DNA and to initiate carcinogenesis. *N*-acetyltransferase (NAT2) may play a role, its rate determined by a polymorphic gene. The results of Ambrosone et al. (1998) were recently confirmed by studies of Delfino, Sinha, and Smith (2001) who did not find a correlation between NAT2 and breast cancer nor any association between the intake of red meat of any doneness and breast cancer.

Genetic polymorphisms including environmental aspects (gene–environment interactions) may also play a critical role in colorectal cancer with respect to red meat intake. Le Marchand (1999) investigated the colorectal cancer rates in Japanese immigrants in Hawaii. The colorectal cancer incidence of these groups (214,000 immigrants between 1886 and 1924) was initially very low and is now the highest in the world. The fast acetylator genotype (NAT2), without the polymorphism is present in 90% of Japanese compared with 45% of Caucasians; the frequency of CYP1A2 phenotype is similar in both groups. Consumption of well-done meat together with a specific genotype of NAT2 and CYP1A2 may increase colorectal cancer risk substantially. Among the Japanese migrants who ate well-done red meat, those without the polymorphisms in both NAT2 and CYP1A2 had a 3.6 times greater risk of developing colon cancer than those with the polymorphisms. Another family of genes might determine individual susceptibility: glutathione transferase M1 (GSTM1) and T1 (GSTT1). Both code for cytosolic enzyme glutathione *S*-transferase which are involved in phase 2 metabolism especially in polycyclic aromatic hydrocarbon metabolism. The results of the few studies dealing with genetic

polymorphisms of GST are inconsistent. Two studies suggest increased colon cancer risk in subjects with high meat intake and GST non-null genotype, contrary to the underlying hypothesis. One study suggests a strong inverse relation between colorectal adenomas and broccoli consumption, particularly in subjects who are GSTM1 null (review, see Cotton, Sharp, Little, & Brockton, 2000). As long as genotypically defined cohorts are not studied with respect to their susceptibility against meat intake (in different forms) the risk of red meat cannot be clearly identified. White meat and fish seem to be without risk, red meat only in a form where cytotoxic by-products such as HCA are formed.

Formation of HCAs can be significantly reduced by inexpensive and practical measures such as avoidance of exposure of meat surfaces to flames, use of aluminium foil to wrap meat before oven roasting and the employment of microwave cooking. Another protecting approach is the combination with protective bioactive constituents derived from plant food. For example, diallyl sulfide an organosulfur compound in garlic, blocks HCA carcinogenesis (Hasegawa, Hirose, & Kato, 1995; Morie, Sugie, Rahman, & Suzui, 1999). Nevertheless, even there may be some induction or promotion factors present in meat, it may depend on the composition of the diet whether anti-carcinogenic factors from plants neutralise any harmful factors in meat. In addition meat contains bioactive constituents known to be protective against cancer formation.

5. Protecting factors in meat with respect to cancer

5.1. Folate

Meat is an important source for methyl donors such as folate and vitamin B12 and transfer factors methionine and choline. Folate and methionine as methyl donors influencing methyl group availability may also be associated with colon cancer incidence. It is frequently argued that the increased risk of different types of cancer resulting from low intake of fruits and vegetables is a result of a folate deficient diet, because fruits and vegetables are important sources for folate. While this is true, however, it has to be considered that the bioavailability of folate from meat and liver is much better than from fruits and vegetables. A few studies measured folate directly and it was claimed that a low folate intake has been related to an increased occurrence of colon adenomas (Benito, Stiggelbout, & Bosch, 1991; Giovannucci, Stampfer, & Colditz, 1993a) and cancer (Freudenheim, Graham, & Marshall, 1991; Lashner, Heidenreich, & Su, 1989). Zhang, Hunter, and Hankinson (1999) studied the effect of alcohol and folate on breast cancer. The increased cancer risk associated with alcohol consumption (>15 g/day) was reduced in women

who consumed at least 300 µg folate/day. The major source of folate was supplements. Even an intake of 300 µg/day does not reach the RDA (400 µg/day) this study shows that increasing the intake might be beneficial with respect to cancer. Indeed, increasing folate intake via supplementation, a form which has a very good bioavailability compared to vegetable-derived folic acid, decreases the risk of colon cancer significantly (Giovannucci, Stampfer, & Colditz, 1993b). The decreased risk, however, was not evident before 15 years, documenting that protective factors, if they indeed exist as single bioactive constituents, need to be present in the diet for a long time period. Vice versa their absence or a low intake might also contribute to an increase cancer risk after a long time period. In rodents, diets deficient of methyl donors or transfer factors (folate, B12, methionine, choline) induce tumours at different sites (Cravo, Maso, & Dayal, 1992; Shivapurkar & Poirer, 1983; Wainfan, Dizik, & Stender, 1989). A methyl deficient diet lowers the concentration of the methyl donor *S*-adenosylmethionine which leads to a reduction in methylation of DNA cytosine. Tumour suppressor genes are inactivated by methylation of normally unmethylated sites. DNA hypomethylation due to a diet low in methyl donors (e.g., low in meat) may contribute to a loss of protooncogene expression (Nyce, Weinhouse, & Magee, 1983). Indeed, throughout the different stages of colonic neoplastic transformation genomic hypomethylation (Goelz, Vogelstein, & Hamilton, 1985) methylation of usually unmethylated sites (Makos et al., 1992) and abnormal elevated DNA methyl transferase activity (Issa, Vertino, & Wu, 1993) is described.

An additional aspect, also involved in methylation reactions, which might contribute to the individual colon cancer risk, is a genetic polymorphism of a key enzyme of folate metabolism: the methylenetetrahydrofolate-reductase (MTHFR). This enzyme converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, the major circulatory form of folate in the body and primary methyl donor for the methylation of homocysteine to methionine. This pathway is a critical key in the methylation process of the DNA. As described above alterations in the methylation process can result in abnormal expression of oncogenes and tumour suppressor genes (Baylin, Makos, & We, 1991). The polymorphism of the human MTHFR gene (alanine to valine substitution, coding for a thermolabile enzyme with reduced activity) results in elevated plasma homocysteine levels. Homozygous individuals have 30% normal enzyme activity, heterozygous 65%. Up to now there are controversial results in correlating this polymorphism with individual colon cancer risk. However, supplementation of folate or a diet rich in folate with optimum bioavailability, lowers homocystein and might therefore influence the individual risk (Bronstrup, Hages, Prinz-Langenohl, & Pietrzik, 1998).

5.2. Vitamin A

The German society for Nutrition recommends an increase in vitamin A intake of 40% for pregnant women and of 90% for breastfeeding women. Pregnant women and those who want to become pregnant are asked to avoid liver for scientifically very weakly proved reasons, therefore the provitamin A-carotenoid β -carotene remains the essential vitamin A source. The most important sources of vitamin A are orange and dark-green vegetables followed by enriched juices, which represent between 20 and 40% of the daily supply. In Germany, the mean intake is about 1.5 and 2 mg of β -carotene a day. If one supposes a conversion rate for β -carotene for juices of 4:1, for fruit and vegetable of 12:1 up to 26:1, this supply leads to a vitamin A supply of 10–15% of the recommendation. Because the liver consumption of the population per head and per year amounts to less than 500 g, β -carotene is an important vitamin A source for young women, especially pregnant women and breastfeeding women.

Studies in Great Britain showed that in the middle and working class, the vitamin A supply can be regarded insufficient. The American Association for Paediatrics called vitamin A one of the most critical vitamins during pregnancy and the breastfeeding period, especially in terms of the function and maturation of the lung. If the vitamin A supply of mother is low, the supply of the fetus and the values of the breast milk, which cannot be compensated by post-natal supplementation, are also low. At the same time one has to keep in mind that there is a relationship between folic acid, vitamin A and iron status and low birth weight. This applies especially to premature babies, which show a direct correlation between the vitamin A supply and the occurrence of complications such as respiratory distress syndrome as one of the most frequent and serious complications.

Taken together the major source of vitamin A is liver, which contributes to approximately 75% to the human vitamin A intake. Concerning a sufficient vitamin A supply, the provitamin A, β -carotene, is of minor importance. Its conversion efficacy seems to be nearer to 1:12 and not 1:6 as frequently mentioned.

Is the supply of vitamin A involved in the individual lung cancer risk? On the basis of a few reports, it is assumed that a “local” vitamin-A-deficiency exists in meta- and dysplastic-areas. Measurements of vitamin-A concentrations in metaplastic areas of the respiratory epithelium and the cervix epithelium proved that vitamin A was no longer to be found, in contrast to the surrounding healthy tissues.

At the moment it is difficult to distinguish between cause and effect. Studies carried-out by Edes and co-workers (Edes, 1991) hint at an induction of metaplasia

caused by a vitamin-A-deficit. These studies showed that a depletion of vitamin-A-ester stores in different tissues (Edes, 1991) is caused by toxins that are present in cigarette-smoke (predominantly polyhalogenated compounds).

Epidemiological evidence supports the assumption that the development of obstructive respiratory diseases (COPD) plays an important role in the cancer mortality of smokers. It was shown that the relative risk for smokers to be affected by lung cancer, when they suffered from obstructive ventilation disorder (FEV 1% <60, respectively, 70) (Skillud, Offord, & Miller, 1987) was significantly higher than that of comparative groups with normal lung-function-parameters.

A survey of the dietary habits within the scope of the “National Health and Nutritional Examination Survey” showed that an inverse correlation (Morabia et al., 1989) exists between vitamin-A-supply, as the only one of 12 examined dietary components, and obstructive respiratory diseases (COPD). COPD increase lung cancer risk significantly. If a diminished supply of vitamin A increases the appearance of obstructive respiratory diseases, a marginal or local vitamin-A-deficit could be responsible for the observed changes of the respiratory mucosa. Such a deficit results in a loss of cilia, an increase of secreting cells and finally the formation of squamous metaplasia (Biesalski, Wellner, Stofft, & Baessler, 1985; Chytil, 1985; Stofft, Biesalski, Zschaebitz, & Weiser, 1992).

Such changes (decrease of ciliated cells with simultaneous increase of the secretion) are noted among smokers (Gouveia, Mathe, & Hercend, 1982; Mathe, Gouveia, Hercend, Gros, & Dorval, 1983) and cause a reduction of the mucociliary-clearance. This reduction of the mucociliary-clearance, associated with an increased adsorption of the respiratory syncytial virus (RSV) (Donelly, 1996), could explain the extraordinarily high morbidity and mortality for respiratory infections of children with vitamin A deficiency in developing countries (Sommer, 1993).

There is sound evidence from experimental studies that the alteration of the respiratory mucosa, caused by the vitamin A deficiency, can be re-differentiated into its functional original epithelium, in vivo as well as in vitro, following vitamin A supply (Biesalski et al., 1985; McDowell et al., 1987a, McDowell, Ben, Newkirk, Chang, & De Luca, 1987b, 1984a, McDowell, Keenan, & Huang, 1984b; Rutten, Wilmer, & Beems, 1988a, Rutten, Wilmer, & Beems, 1988b). Squamous metaplasia of the bronchial mucosa, which occurs in smokers in spite of a sufficient supply with vitamin A as an effect of inhalative noxae could also be reversed through systemic application of high retinoid-concentrations in vitro (Lasnitzki & Bollag, 1982, 1987) and in humans in vivo (Gouveia et al., 1982; Mathe et al., 1983).

5.3. Selenium

Selenium is found largely in grains, fish and meats and enters the food chain through plants at geographically variable rates dependent on selenium concentration of the soil. The best known biochemical role for selenium is as part of the active site of the enzyme glutathione peroxidase (GPx). The metabolic function of this enzyme is vital for cells, as it is part of a mechanism responsible for the metabolism and detoxification of oxygen. It is assumed that GPx can protect DNA from oxidative damage and consequently from mutation leading to neoplastic transformation of cells (Combs & Clark, 1985). At relatively high levels, selenium protects against the action of certain carcinogens in various animal models (Halliwell & Gutteridge, 1989). In vitro and in vivo studies, organic and inorganic selenium has been demonstrated to inhibit proliferation of normal and malignant cells and inhibit tumor growth (Griffin, 1982; Redman, Xu, & Peng, 1997). Apoptosis may result from competition of selenium for S-adenosyl-methionine with ornithine decarboxylase (ODC). ODC activity is indeed critically involved in cancerogenesis. From geographical studies, it is documented that in areas with sufficient selenium concentrations in the diet (depending on selenium concentrations of the soil), there is an inverse relationship between selenium status and cancer (Clark, Cantor, & Allaway, 1991; Schrauzer, White, & Schneider, 1977). Epidemiological studies showed inverse associations of selenium intake or plasma levels and cancers of different sites (prostate, colon, skin etc.). In a recent, double blind, placebo controlled cancer prevention trial 200 µg selenium (approx. three times of the RDA) were given daily to patients with histories of basal and squamous skin carcinoma (Clark et al., 1996). Selenium supplementation did not influence the primary endpoint prevention of recurrent skin cancers, but surprisingly was inversely associated with the incidence of and mortality from total prostate, lung and colorectal cancers. Recently Yoshizawa, Willet, and Morris (1998) reported a strong inverse association of toenail concentration of selenium and prostate cancer risk (65% reduced risk in the highest quintile). Toenail concentration reflect long term intake of selenium with the diet and is consequently influenced by bioavailability. From intervention trials and from epidemiological studies there is now evidence indicating “that substantially increases in the consumption of selenium by men taking 80–90 µg/day or more may have striking impact on prostate cancer rates” (Giovannucci, 1998). Recent surveys indicate that average intake of selenium may be as low as 30–40 µg/day (Rayman, 1997). Intake data, however, do not really reflect the bioavailability. Consequently, the diet has a strong influence on total selenium supply of tissues. Especially in areas with low soil selenium dietary sources containing substantial amounts of selenium with good bioavailability

should be recommended. In the US Selenium is mainly supplied by cereals, breads, meats and meat products. Beef alone is estimated to contribute approximately 17% of the total selenium in the American diet. Two recent studies in humans showed that meat was as good a source of selenium as wheat (van der Torre, van Dokkum, & Schaafsma, 1991) and that SeMet was absorbed more rapidly than selenite in selenium deficient men (Xia, Zhao, & Zhu, 1992). In a recent study the bioavailability of selenium was estimated from various portions of fully cooked commercial cuts of beef, including liver, striploin, round, shoulder and brisket in rats (Shi & Spallholz, 1994). The bioavailability from the beef diets was compared with that of selenium as selenite or L-selenomethionine (SeMet). Liver GPx recovery (after depletion), muscle tissue deposition and plasma levels were taken as markers of bioavailability. Liver GPx-recovery was highest from SeMet > beef muscle > selenite = beef liver. Muscle deposition was highest from SeMet > beef muscle > selenite = beef liver. From these results the authors concluded that the bioavailability of selenium from beef is higher than, or at least equal to, that of selenite and slightly lower than that of SeMet. Taken together meat is an important source for bioavailable selenium.

5.4. Zinc

Zinc is a component of some metalloenzymes and is important for cell growth and replication, osteogenesis and immunity. It may further contribute to the overall antioxidative defence. The primary dietary sources of zinc are red meat, sea food, poultry, grains, dairy, legumes and vegetables (Groff & Grooper, 2000). Lower zinc levels were described in cancer patients (Mellow, Layne, & Lipman, 1983; Rogers, Thomas, & Davis, 1993); others did not find this association (Kabuto, Imai, & Yonezawa, 1994; Kok, Van Duijn, & Hofman, 1988). There is good evidence that zinc may contribute to prostate cancer incidence. Total zinc levels in the prostate are 10 times higher than in other soft tissues (Mawson & Fisher, 1952). Uptake of zinc via a membrane transporter into prostatic epithelial cells is under the control of hormones (testosterone, prolactin) (Costello, Liu, & Zou, 1999). Physiological concentrations of zinc inhibit growth of androgen sensitive and androgen-independent prostate cancer cell lines via cell cycle arrest, apoptosis and necrosis (Iguchi, Hamatake, & Ishida, 1998; Liang, Liu, & Zou, 1999). Epidemiological findings are not consistent and a few studies estimating the effect of supplementation on prostate cancer risk are more or less controversial (for review, see Platz & Helzlsouer, 2001). One important reason for this inconsistency might be the high variability of zinc content of different sources, especially meat and sea food. Furthermore, zinc has a much better bioavailability from meat

than from vegetables (Groff & Grooper, 2000) and other factors, present in the diet may increase (citric acid, histidine, cysteine) or decrease (phytate, oxalate) the absorption of zinc (Groff & Grooper, 2000). Consequently, the use of food questionnaires might not be a suitable approach to measure zinc intake. Adequate biomarkers, at present not available, may help to estimate the individual zinc status and consequently the individual risk. At present, there is no clear cut evidence for a preventive effect of zinc on prostate cancer from epidemiological studies. Some small case control studies indicate low plasma zinc or low prostatic zinc levels in patients with prostate cancer compared with healthy controls (for review, see Platz & Helzlsouer, 2001). An optimum zinc intake can be recommended not only with respect to prevention of prostate cancer, and intakes below RDA should be avoided. One factor contributing to low intake might be a decline in red meat consumption which has been reported in New Zealand (Laugesen & Swimburn, 2000), as well as in UK (Whitehead, 1995), USA (Popkin, Haines, & Reidy, 1989) and Canada (Zafriou, 1985), concomitant with an increase in intakes of unrefined cereals, nuts and legumes. Red meat is a rich source of readily available zinc, whereas cereals contain different levels of phytic acid, a potent inhibitor of zinc absorption. Indeed, the recommendation to decrease or even avoid meat intake may result in a low zinc status as recently documented in women from New Zealand (Gibson, Heath, & Limbaga, 2001). In a cross-sectional study of 330 women, the authors assessed the interrelationship of dietary intakes, biochemical zinc status and anthropometric indices. Changes in food selection patterns (reduction of red meat) were suggested to be responsible for the lower biochemical zinc nutrition. This study is an example that a mixed and balanced diet, including meat and meat products, is the best way to ensure sufficient intake of all essential and potentially cancer preventive components.

Meat consumption, especially red meat, is not carcinogenic per se, even if it contains components which, based on epidemiological and animal experiments, are assumed to contribute to cancer formation. On the other hand, a lot of studies exist which demonstrate a reduced cancer risk in persons with a high intake of fruit and vegetables. As a basis for the preventive effect protecting factors such as carotenoids, flavonoids and further phytochemicals are discussed. Within these fruit and vegetables derived protecting factors folic acid, selenium, zinc and other components are claimed to be preventive candidates. Why should these compounds be less effective if they reach the body via meat being an important source for these compounds? The balance of promoting and protecting factors within the diet is important for the protection against cancer. Furthermore, the IR-hypothesis shows that a nutritional behaviour leading to a metabolic syndrome (high energy, high glycemic

carbohydrates) might favour colon cancer or even cancers from other sites. 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. For many individuals a daily multivitamin that contains folic acid may also be part of a reasonable cancer prevention strategy”.

To improve the “preventive capacity” of an individual, a balanced diet, rich in fruits and vegetables, including meat and meat products in moderate quantities, normal body weight and a reasonable amount of exercise represent the best choice.

6. The importance of meat as a source for micronutrients

The reason why meat is an essential source for some micronutrients is due the fact that meat is either the only source or has a much higher bioavailability for some micronutrients.

Two important micronutrients occur only in meat: vitamins A and B12. Both cannot be compensated for by plant-derived provitamins. Provitamin B12 does not exist and the provitamin A, β -carotene, has to be taken in high amounts due to a poor conversion rate (1:12).

Iron has a higher bioavailability when derived from meat as heme iron than plant-derived iron. Similarly folic acid has a nearly 10-fold higher bioavailability from meat (especially liver) and eggs than from vegetables. Consequently, a low intake of meat (including liver) is associated with a risk for deficiencies in selected micronutrients.

Who needs meat – or: are there groups at risk for a low intake of meat derived micronutrients?

Elderly people are generally considered at risk to develop vitamin and trace element deficiencies, especially regarding the vitamins A, D, E, and folate as well as iron and calcium (Anderson, 2001; Bates et al., 2002; Martins, Dantas, Guimar, & Amorin, 2002; Viteri & Gonzalez, 2002). The multifactorial cause of this health hazard comprise quantitative and qualitative decreased food intake, reduced energy expenditure due to sedentary life style and loss of metabolically active body cell mass, and the development of chronic age-associated disorders.

It was generally assumed that impaired bioavailability of micronutrients was a common problem among elderly. However, the digestive and absorptive capacity of the digestive tract is well retained through ageing and if decreased absorption of macronutrients occurs it is the result of disease rather than ageing itself (Black, 2001). An exception to this rule is the impaired bioavail-

ability of dietary iron due to gastric mucosal atrophy, the occurrence of which is age-related and in many cases could be regarded as a disorder rather than a disease. Nevertheless, the frequently occurring atrophic gastritis in elderly, which also affects vitamin B12 absorption, should be one reason to recommend meat intake in this risk groups.

Adequate nutrition during pregnancy plays an important role in the well-being of mother and child and influences the health of the offspring during childhood and adulthood. Nutritional requirements are increased during pregnancy, but will generally be met by dietary intake and adaptive physiological changes (Draper, Lewis, Malhotra, & Wheeler, 1993). However, the micronutrient status of vitamin D, folic acid, iron, and zinc may become compromised without supplementation (Draper et al., 1993; Fogelholm, 1999; Saletti, Lindgren, Johansson, & Cederholm, 2000) especially when meat is avoided, which can be frequently seen in women in the child bearing age. Folic acid supplementation is generally recommended to decrease the risk of serious births defects. Especially in multiparous women the essential fatty acid status may become impaired and negatively affects the neurological and cognitive development of the offspring (Lowik et al., 1992; Reynolds, 2002).

The micronutrient intake of vegans is easily imbalanced with respect to the recommended dietary allowances. Especially the intake of vitamin B12, riboflavin, and selenium often is inadequate. Even the use of dietary supplements often does not meet the recommended intake of vitamin B12 and selenium (Andersson et al., 1986; Boelsma, Hendriks, & Roza, 2001).

Although it seems obvious that subjects on a weight reduction diet are at risk to develop micronutrient deficiencies, the scientific evidence for this is weak. Most reports include less than fifty subjects and deal with the combination of energy restriction and increase of physical activity, and hence are difficult to interpret (Philipsen-Geerling & Brummer, 2000). The micronutrients at risk appear to be iron, magnesium, zinc, fat soluble vitamins and essential fatty acids. Although a nutritionally adequate low-fat diet seems feasible in a motivated, free-living population (Gassull & Carbe, 2001), data exist which show that a high protein intake even when associated with a higher fat intake might favour weight loss.

A recent meta-analysis of studies dealing with dietary weight loss show that protein rich diets low in carbohydrates and a moderate or high fat content resulted in a better weight loss than diets low in fat and protein and rich in carbohydrates (Bravata et al., 2003). Several factors are suggested to contribute to this increased weight loss: better satiety, higher energy expenditure (thermogenesis), greater loss of fat cell mass.

Energy restricted diets and traditional cholesterol lowering diets are typically focussed on the reduction

of total fat intake while simultaneously increasing the proportion of polyunsaturated fatty acids (PUFA's). However, these PUFA's usually contain high concentrations of n-6 fatty acids and low amounts of n-3 fatty acids. This may have an adverse effect not only on reducing the risk for obesity-related metabolic disorders such as vascular disease and heart rhythm disturbances, but also on the regulation of the intermediary metabolism of brain monoamines such as serotonin, which may lead to impaired mood status and depression (Alonso-Aperte & Varela-Moreiras, 2000).

It is well known that malnutrition is far more common among institutionalized and chronic hospitalized elderly compared to free-living subjects in the community and that the prevalence of malnutrition is associated with the severity of morbidity, functional impairments and mental state (Bates et al., 1997; Koehler et al., 2001; Rasmussen et al., 2000; Selhub, Jacques, Bostom, Wilson, & Rosenberg, 2000). The deficiency affects a broad spectrum of micronutrients, such as the B vitamins, especially B1, B6, folate and B12, vitamin C, vitamin D and E, essential fatty acids and selenium (Bates et al., 1999; Brubacher, Moser, & Jordan, 2000). 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 (Block, Norkus, Hudes, Mandel, & Helzlsouer, 2001; Report on Health and Social Subjects No. 49, 1998). Intervention trials with micronutrient supplementation consisting of zinc and selenium, vitamin C, beta-carotene and alpha-tocopherol were associated with a reduction of infectious events, probably due to the micronutrients administration rather than the supplementation of vitamins (Gey, 1993; Gey, Brubacher, & Staehelin, 1987).

Chronic use of drugs may lead to micronutrient deficiency by decreasing food intake mainly due to impaired appetite or reduced motility of the upper gastrointestinal tract, or by decreasing the bioavailability of micronutrients, for example, cholestyramine which impairs the absorption of fatty acids and fat-soluble vitamins, or by interfering with metabolism. A number of micronutrients, such as zinc and magnesium, play a role in phase I oxidation reactions involved in drug metabolism. Typical examples are the increased folate requirements with chronic use of sulphasalazine, methotrexate, or valproic acid. However, a relevant interaction between drugs and specific micronutrients only occur in case of prolonged use of specific drugs in high doses in susceptible subjects.

7. Selected meat derived micronutrients

Meat is an excellence source for various micronutrients: low-fat pork meat contains 1.8 mg iron, 2.6 mg

zinc, pig liver contains 360 mg magnesium, 20 mg iron and 60 µg selenium per 100 g. Meat and liver (100 g/day) can cover up to 50% of the RDA for iron, zinc, selenium, Vitamins B12, B1, B2, B6 and 100% of vitamin A.

7.1. Vitamin A

Vitamin A is essential for growth and development of cells and tissues. In its active form, retinoic acid, it controls the regular differentiation as a ligand for retinoic acid receptors (RAR, RXR) and is involved in the integration (gap junction formation) of cell formations (Kurokawa, DiRenzo, & Boehm, 1994). Vitamin A plays a substantial role, especially in the respiratory epithelium and the lung. During moderate vitamin A-deficiency, the incidence for diseases of the respiratory tract is considerably increased and repeated respiratory infections can be influenced therapeutically by a moderate vitamin A-supplementation (Pinnock, Douglas, & Badcock, 1986; Sommer, 1993; West, Pokhrel, & Katz, 1991). In addition to the importance of the vitamin for lung function, vitamin A is also responsible for the development of many tissues and cells as well as for the embryonic lung development. Recent studies proved that the control occurs by different expressions of retinoid receptors.

7.1.1. The influence of vitamin A for the maturation and differentiation of the lung

The alveolar cells of type II are especially prepared to synthesize and secrete surfactant (Zachman, 1989). Retinoic acid (RA) is able to stop, concentration-dependently (Metzler & Snyder, 1993) the expression of the surfactant-protein A (SP-A) in human fetal lung explants. Insulin, TGF-β and high concentrations of glucocorticoids can also down-regulate the SP-A-mRNA-expression (Weaver & Whitsett, 1991), but lower concentrations of glucocorticoids are stimulating the expression of these genes (Odom, Snyder, Boggaram, & Mendelson, 1988). In contrast, the SP-B-mRNA-expression is increased in human fetal lung explants both by hyperoxia (rats) (Metzler & Snyder, 1993) and by dexamethason (human fetal lung explant). Consequently, the formation of some surfactant-proteins is regulated differently and selectively by RA together with glucocorticoids.

Prostaglandins of type PGE2 are able to increase the surfactant-synthesis. Under the influence of EGF (epidermal growth factor) the formation of prostaglandin rises, especially of PGE2. On the other hand, the expression of the EGF-receptor is increased by RA. EGF increases the proliferation of the lung tissues and this leads to an amplified formation of surfactant phospholipids (Sundell, Gray, Serenius, Escobedo, & Stahlman, 1980). RA and EGF both lead to an increase (40%,

80%) in PGE₂-secretion in fetal lung cells of rat in vitro (Haigh, D'Souza, & Micklewright, 1989). The combination of RA and EGF though leads to a more than a six-fold increase of the PGE₂-secretion. Consequently, RA can interfere in the lung development by its modulating effect on the EGF-expression and the subsequent PGE₂-induced surfactant formation. A sufficient and continuous availability (either on the blood pathway or by local storage sides) is pivotal, especially for a time-dependent regulation of the lung-development and the related formation of the active metabolite retinoic acid.

7.1.2. Vitamin A-kinetics during fetal lung development

In fibroblast-like cells close to the alveolar cells, in type-II-cells as well as in the respiratory epithelium retinyl-esters, as local extrahepatic stores are present. The importance of these retinyl-esters as “acute reserve” during the development of the lung becomes apparent during the late phase of gestation and the beginning of lung maturation. During this period, a rapid emptying of the retinyl-ester stores in the lung of rat embryos occurs (Geevarghese & Chytil, 1994). This depletion is the result of an increased demand in the process of the lung development, because the retinoic acid is “instantly” needed for the process of cellular differentiation (e.g., proximalization) and metabolic work (surfactant).

The prenatal lung development is also influenced by glucocorticoids. The steroid hormones have a similar effect on lung development to vitamin A, i.e., these two factors complement each other. This is not surprising, because the receptors for steroids and retinoids belong to the same multireceptor-complex. The mode of action of glucocorticoids does not only come into action on the level of gene-expression, but seems to have an impact in a much earlier phase of the vitamin release. The application of dexamethason leads to an increase of the maternal and fetal retinol-binding protein. Thus, the vitamin A-supply is improved via the regular hepatic export pathway. Such an increase of the vitamin-A-concentration in the systemic circulation obviously diminishes morbidity and mortality of prematures due to bronchopulmonary dysplasia (Shenai, Kennedy, Chytil, & Stahlman, 1987, 1990). Dexamethason, respectively, glucocorticoids are not only leading to an improvement of the total vitamin A-supply through a change of the release from the liver, but they also influence, as recently described (Geevarghese & Chytil, 1994), the metabolization of the vitamin A-esters, which are stored in the lung. After administration of dexamethason, as well as after administration of steroids, a significant reduction of retinyl-esters in the maturing lung can be detected, together with a moderate increase of retinol, the hydrolyzation product of retinyl-ester. This observation may explain the therapeutical success with steroids, respectively, also their failures during the therapy of lung-distress-syndrome of prematures. As far as an insuffi-

cient supply is concerned, inappropriate retinyl-ester stores, caused by a shortage of supply of the fetal lung during the late pregnancy, the regulatory effect of glucocorticoids for the vitamin A-metabolism of the lung cells cannot take place.

Very low plasma-vitamin A-levels (Shenai, Chytil, Jhaveri, & Stahlman, 1981) are recurrently found in prematures, especially in cases with lung-distress-syndrome. This can, amongst other things, be attributed to the relative immaturity of the liver for the synthesis of retinol-binding proteins. The neonate is almost exclusively dependent on the mother in its supply, this includes the lung retinyl-esters which are either absorbed by the cells directly (from chylomicrons) or by esterification of retinol after uptake into the cells. These lung retinyl-ester stores can only be sufficiently filled if the mother guarantees an appropriate vitamin A-supply especially during the late pregnancy.

7.1.3. The influence of an insufficient vitamin A-supply on the post-natal development of the lung

A disease seen recurrently in connection with vitamin A-supply is the bronchopulmonary dysplasia (BDP). The pathogenesis of BDP certainly depends on a multitude of factors. Some of the observed morphological changes are very similar to the ones seen in vitamin-A-deficiency of humans and animals. In particular, there is focal loss of ciliated cells with keratinizing metaplasia and necrosis of the bronchial mucosa as well as an increase of mucous secreting cells (Stahlman, 1984; Stofft et al., 1992).

Especially because focal keratinizing metaplasia may occur as a consequence of vitamin-A-deficiency, strengthens the assumption of an impairment of the differentiation on the level of the gene-expression. Since vitamin A regulates the expression of different cytokeratins and therefore influences the terminal differentiation, it seems obvious to suppose common mechanisms. Consequently, the premature but especially the neonates are dependent on a sufficient supply with vitamin A, to ensure the regulation of the cellular differentiation of the respiratory epithelium and lung epithelium. The earlier a child is born before due date, the lower its serum-retinol-levels are (Mupanemunda, Lee, Fraher, Koura, & Chance, 1994). Since a further decrease of the serum-retinol-level and RBP-level occur post-natally, the plasma value at the time of birth is considered to be a critical parameter regarding the lung development.

Repeatedly, it has been shown that serum-retinol-level and RBP-level in prematures are significantly lower than in neonates (Shah & Rajalekshmi, 1984). In the liver of prematures significantly lower retinol levels can be found in comparison to neonates (Shenai, Chytil, & Stahlman, 1985). Plasma values lower than 20 µg/dl are not rare in this case and they should be taken as an indicator of a vitamin-A-deficit.

Reduced plasma levels during the first months of life have a considerable influence on the overall development as well as on the susceptibility of infants to infections. With reduced retinol-plasma-levels, repeated infections are more often described (Barreto, Santos, & Assis, 1994; Filteau, Morris, & Abbott, 1993; Pinnock et al., 1986) and they are counted among the main complications of a poor vitamin A-supply in developing countries. In addition, the serum vitamin A level during infectious diseases, particularly of the respiratory tract, continues to drop (Neuzil et al., 1994). On one hand, this can be explained with an increased metabolic demand and on the other hand with an increased renal elimination of retinol and of RBP during acute infections (Stephensen et al., 1994).

The discussion whether liver as a component of a healthy diet should be avoided is primarily based on questionable contaminants suspected in the liver (e.g., hormones, xenobiotics, metals etc.). If β -carotene from vegetables were the only source of vitamin A, more than 500 g mixed and β -carotene rich vegetables per day must be eaten to reach the recommended 1 mg retinol. Concerning contaminants it has not been evaluated whether this amount of vegetables contains more contaminants than a portion of liver. A small portion of liver (100 g) twice a month is neither toxic nor teratogenic and contributes to a sufficient supply of the body with vitamin A.

7.2. Iron

Iron supports oxidative metabolism. It is essential for gas exchange at the tissue and cellular levels through hemoglobin oxygenation in red cells and myoglobin in skeletal muscle (Beard, Dawson, & Pinero, 1996). Moreover, iron-containing enzymes are involved in cellular energy metabolism and in host-defence responses (Beard et al., 1996; Griffiths, 1996). These various roles are due to the biological catalytic activity of iron. Like many other transition elements, it possesses unfilled atomic orbitals that allow it to co-ordinate electron donors and participate in redox processes (Fraga & Oteiz, 2002; Griffiths, 1996).

Iron is one of the most abundant elements in the Earth's crust, paradoxically, iron deficiency is the most common and widespread nutritional disorder in the world (DeMaeyer & Adiels-Tegman, 1985). Due to biological losses, such as cyclical monthly bleeding of fertile-aged women, excessive infestation with blood-feeding parasites, or poor bioavailability of iron from plant-based diets, it is estimated that as many as 4–5 billion people, 66–80% of the world's population, may be iron deficient (DeMaeyer & Adiels-Tegman, 1985; World Health Organization, 1992). At any given time, 2 billion people – over 30% of the world's population – are anemic, mainly due to iron deficiency, and in developing

countries this is frequently exacerbated by malaria and worm infections (World Health Organization, 1992).

There is a particular risk of iron deficiency for women and girls of child-bearing age, because of menstrual losses. 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 (Beard et al., 1996). In the British National Diet and Nutrition Survey, iron intakes were found to be low in girls (aged 7–18 years), with iron intakes decreasing 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 different bioavailability depends on the presence or absence of different ligands (phytates from cereal products, tannins from coffee and tea and oxalates from vegetables) which form complexes with iron and zinc and block their absorption. A diet which is primarily composed of vegetables, rice, beans and corn is associated with a poor iron bioavailability which at least explains the high incidence of anaemia in developing countries. One hundred grams pork meat added to the vegetarian diet described above increases the iron absorption 3.6-fold.

7.3. Folic acid

In European countries the average folate intake in adults was found to be remarkably similar, around 300 $\mu\text{g}/\text{day}$ in adult males and 250 $\mu\text{g}/\text{day}$ in adult women (De Bree, van Dusseldorp, Brouwer, van het Hof, & Steegers-Theunissen, 2001). This is at about the recommended intake level, but lower than that recommended for pregnant women and women planning a pregnancy. For these groups an intake of >400 $\mu\text{g}/\text{day}$ is considered protective against neural tube defects. More than 90% of women of childbearing age have dietary folate intakes below this optimal level. However, it must be realised that it is difficult to assess dietary folate intake because databases often do not have complete and updated information for folate content of many foods.

The link between poor folic acid status and neural tube defects is well documented but poorly characterized. Poor status is also linked to risen plasma homocysteine, a risk indicator for cardiovascular diseases and poor status may also increase the risk of neurological disorders and cancers. Supplementation with folate (100% bioavailability) reduces risk for neural tube defects up to 70%. Regarding the bioavailability, liver might be also a good source.

7.4. Vitamin B12

Vitamin B12 is found only in animal products. In a recent UK study of 250 vegetarian 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 (130 ng/L) (Lloyd-Wright, Allen, Key, & Sanders, 2000). The elderly 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. There was no difference in mean levels between men and women. However, vitamin B12 intakes were adequate when compared with UK dietary reference values (Finch et al., 1998).

7.5. Selenium

Selenium is often considered as belonging to the group of antioxidant nutrients, since it is incorporated into the enzyme glutathione peroxidase, which acts as a cellular protector against free radical oxidative damage. A secondary end-point analysis of a randomised placebo-controlled skin cancer prevention trial suggested that supplemental selenium might reduce the incidence of and mortality from cancers at several sites (Clark et al., 1996). However, the efficacy of selenium as a cancer preventive agent should await the results of large on-going controlled studies. Selenium is, like many other nutrients, necessary for a well-functioning immune system, and has been pointed out as particularly efficacious in HIV and AIDS. A systematic review found no evidence for a clinical relevant function of selenium in that respect (Ozsoy & Ernst, 1999).

Although selenium is widely distributed in the environment, the selenium content of animal derived foods is greatly affected by soil on which crops grow or animals graze. Recent evidence suggests that selenium intakes in most parts of Europe are falling and are low when compared with recommended intakes (Rayman, 1997, 2000). Declining intakes in the last three decades have been attributed mainly to a change in the source of wheat for bread and cereal products, from predominantly North American to European origin (from a high to low selenium content). These are reflected in decreasing plasma or serum selenium levels. Due to its antioxidant effects, selenium may be protective against chronic degenerative diseases. In the UK, selenium intakes were low in the majority of the elderly (aged 65 and over) in the British National Diet and Nutrition Survey when compared with UK dietary reference values (Thane & Bates, 2001). Selenium intakes decreased with increasing age in this population subgroup. Sufficient zinc intake is important for the proper function of the immune system.

7.6. Zinc

Zinc deficient individuals demonstrate slower wound healing and are more prone to infections. However, studies of the effect of zinc supplementation aimed at the healing rate of venous leg ulcers have been inconclusive. A Cochrane review concluded that oral zinc did not appear to aid the healing of leg ulcers, and that there was only weak evidence that zinc was of benefit in patients with venous leg ulcers and low serum zinc (Wilkinson & Hawke, 2002). Zinc has been found to inhibit rhinovirus replication in vitro. Some studies have demonstrated that zinc may beneficially affect cold symptoms; however, a meta-analysis of randomised controlled trials concluded that the evidence for the effectiveness of zinc in reducing the duration of common cold symptoms is lacking (Jackson, Lesho, & Peterson, 2000). Finally, in settings with high rates of stunting and low plasma zinc concentrations, zinc supplementation may improve children's growth (Brown, Pearson, & Allen, 1998). So far, studies with supplementation did not reveal consistent results. However, a low intake of zinc is associated with a weakened immune system. T-cell-count, T-cell-proliferation- and function and NK-cell activity are reduced. Especially in elderly a reduced zinc status is evident (Lukito, Wattanapenpaiboon, Savage, Hutchinson, & Wahlqvist, 2004). In elderly a higher protein intake (together with slight exercise) stops sarcopenia, a progressive loss of lean body mass. During pregnancy and lactation a higher need of zinc is documented as well as during chronic inflammatory diseases (Rink & Gabriel, 2000).

8. Conclusion

Meat as a component of a mixed and healthy diet contains important and essential micronutrients. The adequate intake ensures a normal function of the immune system, the mucous membranes and the general metabolism of substrates. At least a sufficient intake ensures that during time periods of higher need e.g., diseases, pregnancy, this need is adequately covered. Especially in risk groups (elderly, pregnant women, growing children) meat should be consequently recommended.

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