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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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Introduction

Meat is frequently associated with a “negative” health image due to a “high” fat content or in cases of red meat as a cancer promoting nutrient. Therefore a low meat intake, especially red meat is recommended to avoid risk for cancer, overweight and at least metabolic syndrome. However, this discussion overlooks the fact, that meat is an important source for a couple of 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 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, 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 micronutrient source, 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 be preventive with respect to 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.

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 and Cambell, 1998). However the majority of epidemiological cohort and case control studies could not confirm these assumptions. Only for red meat derived protein there is some evidence that risk increases if red meat is part of the diet twice a day and more (MacIntosh and Le Reu, 2001) or processed (cooked 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 really understood. McIntosh and co workers observed a non significant increase from 33% to 59% in incidence of mature rats with DMH-induced intestinal tumours when barbecued beef was substituted for whey protein concentrate against a high fat (20%) diet background (MacIntosh et al., 1998). Whether the concentration of protein in a diet determines the risk for cancer is controversially discussed (MacIntosh and Le Reu, 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 for colon cancer. It was hypothesised that IR leads to increased initiation and promotion of colon cancer by an elevated serum insulin as a growth factor or raised glucose and triglycerides as fuels (McKeown-Eyssen 1994). Bruce and co workers (Bruce et al., 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 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 et al., 1998). Red meat however, have 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 and co-workers (1997) showed that IR rats on a high fat diet promotes aberrant crypt formation (ACF) 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 w3-fatty acids could be deleterious affecting cell signalling in colonic cells in ways that lead to IR and colon cancer. Dietary intervention that reduce IR may also reduce colon cancer risk. So far low fat meat seems not to contribute to colon cancer.

Fat

Several epidemiological early case control and cohort studies suggested a positive correlation between fat intake and incidences of breast-, colon- and prostate cancer (Schottenfeld and Fraumeni, 1996; Potter et al., 1993). 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 (Howe et al., 1997; Giovannucci et al., 1994). 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 et al., 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. 16 out of 22 case control or cohort studies showed an increased risk above a risk ratio of 1.3. A recent prospective study (Michaud et al., 2001) documented an elevated risk for prostate cancer (RR 1.47) and 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 have been observed primarily for PUFA (Hopkins and Carroll, 1979; Hopkins et al., 1981). A couple of studies show that polyunsaturated w6 fatty acids (linoleic acid) enhance cancer development in rodents (Carroll 1991; Fay et al., 1997). The prostaglandin E2 (PGE2) seems to be involved in colon carcinogenesis and is formed from w6 fatty acids (arachidonic acid). EP1 (PGE2-receptor) k.o. mice showed resistance to AOM induction of neoplastic colon lesions (Watanabe et al., 1999). w3 fatty acids (linolenic acid) however, suppress colon carcinogenesis by inhibiting the arachidonic pathway (Takahashi et al., 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 controverse results from



different studies and the fact that meta analyses show that fat might be a rather minor component, 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. So 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 et al., 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 reesterification of triglycerides may also play important roles regarding the individual susceptibility. Finally, components not belonging to lipids might contribute to carcinogenesis such as HCAs or at least the iron content of meat. Dietary iron enhances lipid peroxidation in the mouse colon (Younes et al., 1990) and increases the incidence of DMH-induced colorectal tumours in mice and rats (Siegers et al., 1988; Nelson et al., 1989). Indeed, studies in humans point on an relationship between body iron stores and the incidence of colon tumours (Stevens et al., 1988; Knekt et al., 1994a). 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.

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 et al., 1998) and some negative (Augustsson et al., 1999) links between cancer risk and intake of welldone meat or fish. Studies that have examined intensity of cooking have tended to show positive associations with breast cancer (Knekt et al., 1994b), others not (Ambrosone et al., 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 and coworkers (Ambrosone et al., 1998) were recently confirmed by studies of Delfino and coworkers (2001) who did not find neither a correlation between NAT2 and breast cancer nor any association between red meat intake for 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 group (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 a welldone 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 nonnull 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 et al., 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 were cytotoxic by-products such as HCA are formed.

Formation of HCAs can be significantly reduced by inexpensive and practical measures like avoidance of exposure of meat surfaces to flames, usage 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 et al., 1995; Morie et al., 1999). Nevertheless, even there may be some induction or promotion factors in meat it may depend on the composition of the diet whether anticarcinogenic factors from plants neutralise any harmful factors in meat. In addition meat contains bioactive constituents known to be protective against cancer formation.

Protecting factors in meat with respect to cancer

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 been associated with colon cancer incidence. It is frequently argued that the increased risk for 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. Indeed, 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 (Giovannucci et al., 1993a; Benito et al., 1991) and cancer (Freudenheim et al., 1991; Lashner et al., 1989). Zhang and coworkers (1999) studied the effect of alcohol and folate on breast cancer. The increased cancer risk associated with alcohol consumption (>15g/day) was reduced in women who consumed at least 300µg folate/day. The major source of folate were supplements. Even an intake of 300µg/day does not reach the RDA (400µg/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 risk for colon cancer significantly (Giovannucci et al., 1993b). The decreased risk however was evident not 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 there 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 (Shivapurkar and Poirer, 1983; Wainfan et al., 1989; Cravo et al., 1992). 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 et al., 1983). Indeed, throughout the different stages of colonic neoplastic transformation genomic hypomethylation (Goelz et al., 1985) methylation of usually unmethylated sites (Makos et al., 1992) and abnormal elevated DNA methyl transferase activity (Issa et al., 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 Methylene tetrahydrofolate reductase (MTHFR). This enzyme converts 5,10- methylene tetrahydrofolate to 5- methyl tetrahydrofolate, 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 et al., 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 controverse results in correlating this polymorphism with individual colon cancer risk. However, supplementation of folate or a diet rich in folate with optimum bioavailability lower homocystein and might therefore influence the individual risk (Bronstrup et al., 1998)

Vitamin A

The German society for nutrition recommends the increase in vitamin A intake for pregnant women by 40% and for breastfeeding women by 90%. Pregnant women or those who want to become pregnant are asked to avoid the intake of liver out of very unsure scientifically proved reasons, therefore the provitamin A-carotenoid β-carotene stays the essential vitamin A source. The most important bearers of vitamin A are



orange and deep green vegetable followed by enriched juices, which represent between 20 and max. 40% of the daily supply. In Germany the intake in the mean is by 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, therefore this supply leads to a vitamin A sufficiency of 10 to 15%. Because the liver consumption of the population per head and per year amounts less than 500 g, β -carotene is an important vitamin A source for young women and especially pregnant women and breastfeeding women.

Studies from Great Britain showed that in the middle and working class the vitamin A supply can be seen as insufficient. The American association for paediatrics called vitamin A as one of the most critical vitamins during pregnancy and the breastfeeding period, especially in terms of the lung function and its maturation. If the vitamin A supply of the mother is too low, the supply of the fetus is too low too and also the values of the mother's milk which can't be compensated by postnatal supplementation. 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 earlyborn's which show a direct correlation between the vitamin A supply and the turn up of complications like the respiratory arrest syndrom, as one of the most frequent and serious complications.

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 cleavage efficacy seems to be nearer to 1:12 and not 1:6 as frequently mentioned. Beside its well known effects in the visual cycle vitamin A plays an important role especially in mucous membranes.

Is a sufficient 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 actually proved that vitamin A, in contrast to the surrounding healthy tissues, was no longer to be found.

At the moment it is difficult to distinguish between cause and effect. Studies carried-out by Edes and co-workers (Edes, 1991) hint to 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 plays an important role in the scope of 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 (Melvyn et al., 1987) respectively 70) (Skillud et al., 1987), was significantly higher than that of comparative groups with normal lung-function-parameters.

A survey about 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 obstructive respiratory diseases (COPD) and vitamin-A-supply as the only one of 12 examined dietary components. COPD however, increases 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 (Stofft et al., 1992; Chytil, 1985; Biesalski et al., 1985).

Such changes (decrease of ciliated cells with simultaneous increase of the secretion) are noted for smokers (Gouveia et al., 1982; Mathe et al., 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) (Donnelly, 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 redifferentiated into its functional original epithelium, in vivo as well as in vitro, following vitamin-A-supply (Biesalski et al., 1985; McDowell et al., 1984a,b, 1987a,b; Rutten et al.,



1988 a,b). 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 (Lasnitzky and Bollag, 1982; 1987) and in humans in vivo (Gouveia et al., 1982; Mathe et al., 1983).

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 are 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 the DNA from oxidative damage and consequently from mutation leading to neoplastic transformation of cells (Combs and Clark, 1985). At relatively high levels selenium protects against the action of certain carcinogens in various animal models (Halliwell and Gutteridge, 1989). In 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 et al., 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 (Schrauzer et al., 1977; Clark et al., 1991). 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 200µg selenium (approx. 3 time 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 was surprisingly inversely associated with the incidence of and mortality from total prostate, lung and colorectal cancers. Recently Yoshizawa and co workers (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 the intervention trial and from epidemiological studies there is now evidence indicating "that substantial increases in the consumption of selenium by men taking 80-90µg/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 30-40µg/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 is wheat (van der Torre et al., 1991) and that SeMet was absorbed more rapidly than selenite in selenium deficient men (Xia et al., 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 and 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 this 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.

Zinc

Zinc is a component of a couple of 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 and Gropper, 2000). Lower zinc levels were described in cancer patients (without answering the question of cause or consequence) (Mellow et al., 1983; Rogers et al., 1993); others did not find this association (Kok et al., 1988; Kabuto et al., 1994). There is good evidence that zinc may critically contribute to prostate cancer incidence. Total zinc levels in the prostate are 10 times higher than in other soft tissues (Mawson and Fischer



1952). Uptake of zinc via a membrane transporter into prostatic epithelial cells is under the control of hormones (testosterone, prolactin) (Costello et al., 1999). Physiologic concentrations of zinc inhibit growth of androgen sensitive and androgen-independent prostate cancer cell lines via cell cycle arrest, apoptosis and necrosis (Iguchi et al., 1998; Liang et al., 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 and 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 and Groopner, 2000) and other factors, present in the diet may increase (citric acid, histidine, cysteine) or decrease (phytate, oxalate) absorption of zinc (Groff and Groopner, 2000). Consequently, the use of food questionnaires might not be a sufficient 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 and Helzlsouer, 2001). An optimum zinc intake can be recommended not only with respect to prevention 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 and Swimburn, 2000), as well as in UK (Whitehead, 1995), USA (Popkin, 1989) and Canada (Zafiriou, 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 et al., 2001). In a cross sectional study of 330 women the authors assessed the interrelationship among dietary intakes, biochemical zinc status and anthropometric indices. Changes in food selection patterns (reduction of red meat) were suggested to be responsible for a lower biochemical zinc nutriture. This study shows exemplarily 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.

Conclusion:

Meat consumption, especially red meat, is not per se carcinogenic, even it contains components which, based on epidemiological and animal experiments, are assumed to contribute to cancer formation. On the other hand 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 less effective if they reach the body via meat as an important source? 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, 2000) 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 is the best choice.

The importance of meat as a source for micronutrients

The reason for the importance of meat as an essential source for a couple of micronutrients is due the the fact that meat is either the only source or has a much higher bioavailability.

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



With respect to iron, iron has a higher bioavailability when derived from meat as hem iron than plant derived iron. Similarly folic acid has a nearly ten-fold higher bioavailability from meat (especially liver) and eggs than from vegetables. Consequently a low or near to zero 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 (Martins, Dantas, Guimar, Amorin, 2002; Bates et al., 2002; Anderson, 2001; 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 metabolic 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 malabsorption of macronutrients occurs it is the result of a disease rather than ageing itself (Black, 2001). An exception to this rule is the impaired bioavailability of dietary iron due to gastric mucosal atrophy which occurrence 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 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, Lewis, Malhotra & Wheeler, 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 birth defects. Especially in multifarious women the essential fatty acid status may become impaired and negatively affects the neurological and cognitive development of the offspring (Lowik, van den Berg, Schrijver, Odink, Wedel & Houten, 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 (Boelsma, Hendriks & Roza, 2001; Andersson et al., 1986).

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 & Cabre, 2001), data exist which show that a high protein intake even when associated with a higher fat intake might favor 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 discussed 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 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, Mansoor, van der



Pols, Prentice, Cole & Finch, 1997; Selhub, Jacques, Bostom, Wilkin & Rosenberg, 2000; Rasmussen, Ovesun, Bulow, Kudesn, Laurberg & Perrild, 2000; Koehler, Baumgartner, Garry, Allen Stabler & Rimm, 2001). 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 (Brubacher, Moser & Jordan, 2000; Bates, Prentice et al., 1999). 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, Brubacher & Staehelin, 1987; Gey, 1993).

Chronic use of drugs may lead to micronutrient deficiency by decreasing food intake mainly due to impaired appetite or upper GI motility, 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 (Gregory, Foster, Tyler & Wiseman, 1990). 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.

Selected meat derived micronutrients

Meat is an excellence source for different micronutrients: Low fat pork meat contains 1.8mg iron, 2.6mg zinc, pig liver contains 360mg magnesium, 20mg iron and 60µg selenium per 100g. Meat and liver (100g/day) can cover up to 50% of the RDA for iron, zinc, selenium, Vitamins B12, B1, B2, B6 and 100% of vitamin A.

Vitamin A

The German society for nutrition recommends the increase in vitamin A intake for pregnant women by 40% and for breastfeeding women by 90%. Pregnant women or those who want to become pregnant are asked to avoid the intake of liver out of very unsure scientifically proved reasons, therefore the provitamin A-carotenoid β -carotene stays the essential vitamin A source. The most important bearers of vitamin A are orange and deep green vegetable followed by enriched juices, which represent between 20 and max. 40% of the daily supply. In Germany the intake in the mean is by 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, therefore this supply leads to a vitamin A sufficiency of 10 to 15%. Because the liver consumption of the population per head and per year amounts less than 500 g, β -carotene is an important vitamin A source for young women and especially pregnant women and breastfeeding women.

Studies from Great Britain showed that in the middle and working class the vitamin A supply can be seen as insufficient. The American association for paediatrics called vitamin A as one of the most critical vitamins during pregnancy and the breastfeeding period, especially in terms of the lung function and its maturation. If the vitamin A supply of the mother is too low, the supply of the fetus is too low too and also the values of the mother's milk which can't be compensated by postnatal supplementation. 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 earlyborn's which show a direct correlation between the vitamin A supply and the turn up of complications like the respiratory arrest syndrom, as one of the most frequent and serious complications.

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 cleavage efficacy seems to be nearer to 1:12 and not 1:6 as frequently mentioned. Beside its well known effects in the visual cycle vitamin A plays an important role especially in mucous membranes.



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 et al., 1994; Morree, 1992). 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 et al., 1986; Sommer, 1993; West et al., 1991). In addition to the importance of the vitamin for the 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 as well as by time-dependent changes of the vitamin A-metabolism respectively via cellular vitamin A-binding proteins (CRBP: cytoplasmatic retinol binding protein; CRABP: cytoplasmatic retinoic acid binding protein).

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 the surfactant (Zachman, 1989). Retinoic acid (RA) is able to stop, concentration-dependently (Metzler and 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 and Whitsett, 1991), but lower concentrations of glucocorticoids are stimulating the expression of these genes (Odom et al., 1988). In contrast, the SP-B-mRNA-expression is increased in human fetal lung explants both by hyperoxia (rats) (Metzler and 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 et al., 1980). RA as well as EGF are both leading to an increase (40%, 80%) of the PGE₂-secretion in fetal lung cells of the rat in vitro (Haigh et al., 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.

Vitamin-A kinetic 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 storage's in the lung of rat embryos occurs (Geevarghese and 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 as vitamin A resp. the two factors complement each other. This is not surprising, because the receptors for steroids and retinoids belong 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 diminishes obviously the morbidity and mortality of prematures due to bronchopulmonary dysplasia (Shenai et al., 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 and 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 insufficient 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 et al., 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.

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 (Stahlmann, 1984; Stofft et al., 1992).

Especially focal keratinizing metaplasia, as it may occur after a vitamin-A-deficiency, is strengthening 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 neonate 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 et al., 1994). Since a further decrease of the serum-retinol-level and RBP-level occur postnatally, the plasma value at the time of birth, is considered to be a critical parameter regarding the lung development.

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

Reduced plasma levels during the first months of life have got 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 (Barretto et al., 1994; Filteau et al., 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 the 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).

Conclusion:

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 arriving from vegetables would be the only source of vitamin A we must eat more than 500g mixed and β-carotene rich vegetables per day to reach the recommendations of 1mg 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 (100g) twice a month is neither toxic nor teratogenic and contributes to a sufficient supply of the body with vitamin A.



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-defense responses (Beard, Dawson & Pinero, 1996; Griffiths, 1996). These various roles are due to iron's biological catalytic activity. Like many other transition elements, it possesses unfilled atomic orbitals that allow it to coordinate electron donors and participate in redox processes (Griffiths, 1996; Fraga & Oteiz, 2002).

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

Iron deficiency is a particular risk 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 [62]. 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 with UK dietary reference values. Dietary supplements made no difference to mean intakes and iron status was also low in these groups. Depending on the composition of the individual diet the bioavailability of iron can differ 5 to 10-fold (lit 8 und 9 aus fleisch und gesundheit). 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 out of vegetables, rice, beans and corn is associated with a poor iron bioavailability which at least explains the high incidence of anemia in developing countries. 100g pork meat added to the above described vegetarian diet increases the iron absorption 3.6 fold.

Folic acid

In European countries the average folate intake in adults was found to be remarkably similar, around 300 µg/day in adult males and 250 µg/day in adult women (De Bree, van Dusseldorp, Brouwer, van het Hof & Stegers-Theunissen, 1997). This is about the recommended intake level, but lower than recommended for pregnant women and women with pregnancy wish. For these groups an intake of >400 µg/day is considered protective against neural tube defects. More than 90% of women in the 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 raised 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.

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, 2001). 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).



Selenium

Selenium is often considered as belonging to the group of antioxidant nutrients, since it is incorporated into the enzyme glutathion 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 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; Rayman, 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.

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 et al., 2004). In elderly a higher protein intake (together with slight exercise) stops sarkopenia, 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 and Gabriel, 2000).

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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