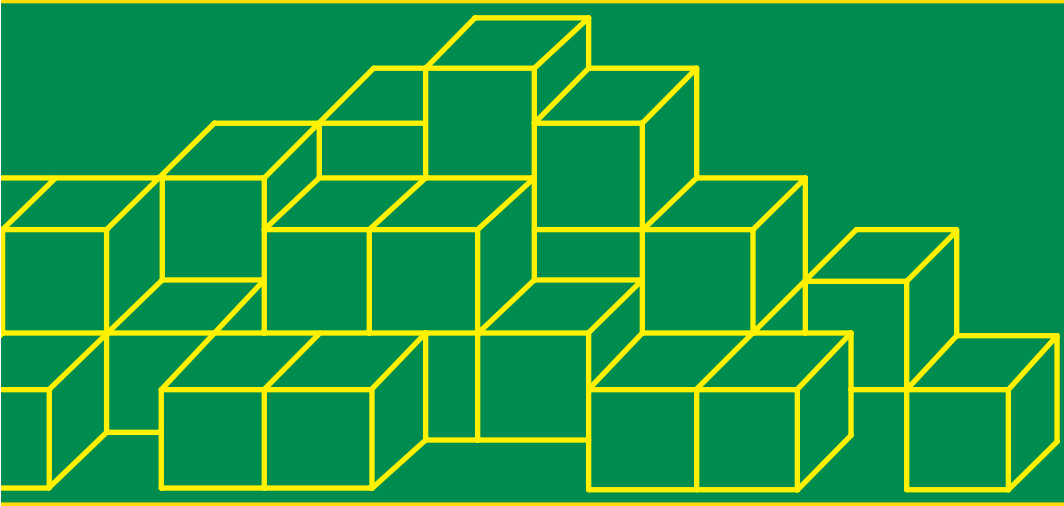
Reference Values for Nutrient Intake

1st edition

German Nutrition Society (DGE)
Austrian Nutrition Society (ÖGE)
Swiss Society for Nutrition Research (SGE)
Swiss Nutrition Association (SVE)



German Nutrition Society

Reference Values for Nutrient Intake

Reference Values for Nutrient Intake

1st edition

German Nutrition Society (DGE)
Austrian Nutrition Society (ÖGE)
Swiss Society for Nutrition Research (SGE)
Swiss Nutrition Association (SVE)

Die Deutsche Bibliothek - CIP-Cataloguing-in-Publication-Data

REFERENZWERTE FÜR DIE NÄHRSTOFFZUFUHR / REFERENCE VALUES FOR NUTRIENT INTAKE / German Nutrition Society (DGE)
[Design and development: Working group 'Reference values for nutrient intake'].
– 1st edition in German – Frankfurt/Main: Umschau/Braus, 2000
ISBN 3-8295-7114-3

Editors
German Nutrition Society (DGE)
Austrian Nutrition Society (ÖGE)
Swiss Society for Nutrition Research (SGE)
Swiss Nutrition Association (SVE)

Design and development
Working Group 'Reference values for nutrient intake'

Translation
Sybill Saupe, Karlsruhe, Germany; Stewart Truswell, Sidney, Australia

Editorial office English translation
Anja Brönstrup, Eva Leschik-Bonnet, Birte Annika Peterson

Layout
Petra Weitz, Wald-Michelbach, Germany

Printing and processing
Druckerei V + V, Bonn

1st edition in English 2002
ISBN 3-8295-7114-5

Printed on chlorine-free paper

Contents

Preface

Much has changed in the fields of nutritional and food sciences since the last edition of the 'Recommendations for Nutrient Intake' of the DGE appeared nearly ten years ago. Advances in molecular biological research allow a better understanding of relationships. Certain nutrients have become the focus of scientific attention; among them are non-nutritive bioactive substances. For these secondary bioactive phytochemicals the first databanks are now being established. Current editions of the nutrient tables by Souci-Fachmann-Kraut and of the *Bundeslebensmittelschlüssel* (German Nutrient Food Code and Data Base) are two extensive sources of the information on nearly all foods.

On the other hand, there are still many gaps in our knowledge. Data on human requirements for essential nutrients are far from complete. Preventive effects of nutrients, dietary nutrient bioavailability and effects of high-dose nutrients are also fields of research still waiting to be thoroughly explored.

For assessment of the quality of our foods and our nutrition, reference values for nutrients are an essential basis. Reference values, moreover, are part of the foundation for food-related nutritional recommendations and for consumer education, counselling and motivation towards wholesome nutrition.

The new reference values now presented have for the first time been developed in collaboration with the nutrition societies in Austria and Switzerland. The term 'Recommendations' in the title of the previous editions has been replaced with the more generic term 'Reference values'; this, however, is only one of many innovations which will be explained in more detail in the introduction and the individual chapters.

The new edition, we are sure, is worth all the time and effort required to produce a comprehensive account of the present state of the science as a source of information for planning adequate diets and for the much needed prevention of nutritional diseases.

We are grateful to everyone who worked on this edition for their very constructive and creative cooperation. We should like to say a special word of thanks to the working group 'Reference values for nutrient intake' and in particular Professor Günther Wolfram, who took on the difficult task of coordinating the work, for his untiring effort and encouragement at all stages of the project. We are also grateful to Dr. Eva Leschik-Bonnet, who for once again supervised the scientific secretariat so carefully.

Frankfurt, Vienna and Basel, March 2000

Professor Helmut Erbersdobler
President, German Nutrition Society

Professor Ibrahim Elmadfa
President, Austrian Nutrition Society

Professor Ulrich Keller
President, Swiss Society for Nutrition Research

Professor Paul Walter
President, Swiss Nutrition Association

Introduction

The present edition of the 'Reference Values for Nutrient Intake', a revised and up-dated version of earlier recommendations published in Germany [1, 2], has - for the first time - been jointly edited by the nutrition societies in Germany (DGE), Austria (ÖGE) and Switzerland (SGE/SVE). Its short name 'D-A-CH Reference Values' has been derived from the common international abbreviations D for Germany, A for Austria and CH for Switzerland. The new edition was given the more generic title 'Reference Values for Nutrient Intake' because 'recommendation' is now exclusively reserved for the recommended intake of a certain nutrient. Therefore the term 'reference values' embraces recommendations, estimated values and guiding values.

Nutrient and energy data in the tables, like those of comparable expert groups in other countries (e.g. Dietary Reference Intakes [DRI] of the United States and Canada [5] or FAO/WHO [4]) provide the basis for practical realization of wholesome nutrition. Reference values refer to the amounts of nutrients that should be present in foods as they are eaten. In principle, requirements have been determined and recommendations derived according to common international methodology [3, 4, 5]. Advice on the use of nutrient tables (previously part C) has been omitted because experience has shown that the figures in parts A and C led to confusion and because common computer programs now consider preparation losses anyway.

The purpose of these nutritional reference values (recommendations, estimated values, guiding values) is to maintain and promote health and the quality of life. In the sense of WHO and FAO [4] they are to ensure the vital metabolic, physical and psychic functions in nearly all healthy individuals of the population. Intake corresponding to the reference values can contribute to prevent nutrient-specific deficiency diseases (e.g. rickets, scurvy, pellagra) and deficiency symptoms (e.g. dermatitis, ophthalmic or cerebral disorders) but also to avoid oversupply with energy or certain nutrients such as fat or alcohol. This is a traditional part of the health-related aims of nutritive recommendations.

In recent years evidence has been increasing that certain nutrients could have effects beyond the prevention of deficiency diseases. As far as possible, these aspects had already been considered in the 1991 edition of 'Recommendations for Nutrient Intake' [2], e.g. for vitamin C, ß-carotene, calcium and dietary fibre although even today there is no definitive answer to the question of whether the nutrients per se are decisive or the composition of the food in which they are contained. In any case, these nutrients can serve as 'reference substances' of protective effects.

Much greater attention is now being given to the effects of nutrients such as vitamin E, ß-carotene and selenium, or also of phytochemicals such as flavonoids or phytooestrogens which are assumed to enhance the body's antioxidative capacity and immune system and so to protect against degenerative diseases such as atherosclerosis and cancer. Furthermore, there has been evidence for the effect of folic acid in preventing neural tube defects and on hyperhomocysteinaemia as independent risk factor for atherosclerosis. Recent observations also suggest a protective effect of vitamin K against osteoporosis.

Previously, the latter connections were generally not taken into account as such delayed effects have only become detectable by modern epidemiological methods. In the present edition they are - for the first time - separately included in section II 'Preventive aspects of nutrients and food components'. On the one hand this should demonstrate their importance for a wholesome diet and on the other makes some space for discussion of their modes of action and effective doses.

References

[1] Deutsche Gesellschaft für Ernährung (ed.): Empfehlungen für die Nährstoffzufuhr der DGE, 5. Überarbeitung 1991 - Kommentar zu den Neuerungen. Ernährungs-Umschau 38 (1991), 479-483

[2] Deutsche Gesellschaft für Ernährung (ed.): Empfehlungen für die Nährstoffzufuhr. 5. Überarbeitung. Umschau Verlag, Frankfurt/Main (1991)

[3] National Research Council: Recommended Dietary Allowances. 10th edition, National Academy of Sciences, Washington D.C. (1989)

[4] WHO (World Health Organisation): Energy and protein requirements. Report of a Joint FAO / WHO / UNU Expert Consultation. WHO Technical Report Series No. 724, Geneva (1985)

[5] Yates, A. A., Schlicker, S. A., Suitor, C. A.: Dietary Reference Intakes: The new basis for recommendations for calcium and related nutrients, B vitamins, and choline. J. Am. Diet. Assoc. 98 (1998), 699-706

Section I: Nutritive aspects of nutrients

In the individual chapters, 'reference values' are presented in the following way:

Part A: Reference values – summary tables
Part B: Explanations of the reference values

Reference values, except for the guiding values for energy, stand for amounts judged to be high enough to protect practically any healthy person in a defined group against nutritional impairment of health and to ensure fitness. They are, furthermore, intended to produce certain body reserves which in case of sudden increased needs are immediately available without impairment of health. Experience has shown that this applies to healthy individuals in Central Europe. For the physiological and biochemical fundamentals, see references [1, 2, 8, 9, 10, 17, 20, 21, 23, 29, 32, 33, 35]. In the United States and Canada, 'Dietary Reference Intakes' (DRI) were and still are being established [14, 15, 37]. They are referred to in the individual chapters, as far as they have been published.

The present reference values do not refer to the care of sick and convalescent people. They are - except for iodine - not sufficient to replenish depleted stores in individuals with nutrient deficiencies. Nor do they apply to individuals with indigestion and metabolic disorders or to addicts (e.g. high alcohol consumption) or to persons with extra needs due to regular medication. For this group, individual dietary advice and medical care are needed. This applies also to the prevention of damage and complications of diseases.

Reference values: Recommendations, estimated values and guiding values

Energy and nutrient requirements differ from individual to individual and from day to day; they depend on all sorts of endogenous and exogenous influences. Experimentally, requirements can only be determined in defined and small population groups; the data obtained are subject to statistical variations. In the presence of a normal (Gaussian) distribution, energy and nutrient intake corresponding to the group's 'average value' will meet requirements of 50% of all the subjects investigated, while those of the remaining 50% will not be met.

For *energy intake*, it was decided that the reference value should always be the group's average requirement; this decision is in line with nutritional policy in Germany, Austria and Switzerland where protection against overnutrition is given priority over concerns about insufficient supply. Hence the reference values for energy are average requirements for each group, and not reference values for each individual in the group. The energy expenditure of individuals is greatly influenced by physical activity, and also by sex and body mass. Energy

requirements of individuals can only be determined by regular body weight checks. Information about energy requirements for different age and occupational groups is only provided in terms of average values intended for use in calculations (e.g. of nutrient density or for catering and supplying communities). The energy requirement data shown below are based for the first time on measurements using the doubly (stable) labelled water method (DLW) ($^2H_2{}^{18}O$); hence they are not comparable to data available previously. They apply to individuals of normal weight (see table 1, page 21) and with corresponding physical activity. In accordance with international standards, they are based on the basal metabolic rate and include common physiological allowances (physical activity level = PAL, see table 3, page 23) as multiples of the basal metabolic rate.

To obtain recommended intakes for *essential nutrients*, values of average requirements, taking bioavailability into account, would have to be increased by two standard deviations assuming a normal distribution. These amounts should cover the needs of nearly 98% of the population and protect against deficiency related damage to health. For several reasons, however, this procedure is not generally practicable. Except for protein, nutrient requirements are not known to follow a statistically normal distribution; frequency distribution data on requirements are only available for individual nutrients and for very small population groups. Partly as an alternative to requirement data, one has to resort to data obtained in long-term surveys of the actual essential nutrient status of population groups. Hence fundamental information to determine **average requirement** is of diverse origin and cannot always be assessed the same way. Consequently, instead of two standard deviations, increasing average requirement by 20 - 30% should give an acceptable estimate for setting reference values for a group. This increase is based on an assumed coefficient of variation of 10 - 15%; it is comparable in extent to the hypothetical two standard deviations.

The reference values for thiamin, riboflavin and niacin are based on the reference values for energy. In children, the values of table 4 (page 26), in adolescents and adults those in table 5, with PAL 1.4 (page 27) are used. In children reference values for energy, due to usually greater physical activity, exceed those for adults with sedentary occupations, and so reference values for thiamin, riboflavin and niacin in boys aged 13 - 15 years are above those of adolescents and adults. The estimated values for vitamin E are analogously derived from the values for energy intake in combination with those for fat and unsaturated fatty acid intake. The recommended intake of vitamin B_6 is derived from the recommendations for protein intake.

The recommended intakes are expected to allow for individual physiological variability and to ensure sufficient nutrient reserves in the body. In those frequent cases in which recommendations could not be made for every age group, values for intermediate age groups had to be interpolated. **Recommendations**

(*Empfehlungen* or RDA in the DRI) are expressed for protein, n-6 fatty acids, and most of the vitamins, minerals and trace elements.

For some nutrients (n-3 fatty acids, vitamin E, vitamin K, ß-carotene, biotin, pantothenic acid and some trace elements), human requirements cannot yet be determined with desirable accuracy. In these cases **estimated values** (*Schätzwerte*) were made using data that, though supported by experiment and mostly derived from intakes of healthy, well nourished groups, have not been adequately validated. Either the measured values varied excessively for methodological reasons, or human studies yielded insufficient or unsatisfactory results. However, the estimated values still provide appropriate information for adequate and safe intake. As far as possible, estimated values are given in precise figures, not in ranges. For some trace elements (copper, manganese, selenium, chromium, molybdenum) and ß-carotene and biotin, however, the available data allow only ranges to be specified. For sodium, chloride and potassium, estimated values are for minimum intakes.

Guiding values (*Richtwerte*), meaning aids for orientation, are given in those cases in which some - less stringent - regulation of intake is necessary for health reasons. Accordingly, a desirable lower limit is set for water, fluoride and dietary fibre, and an upper limit for total fat, cholesterol, alcohol and table salt (sodium chloride).

Use of the reference values

For correct use of the reference values it should be stressed that nutrients providing energy and essential nutrients are judged differently, and that recommendations, estimated values and guiding values are given different weightiness.

A recommendation, according to its definition, meets the requirement of nearly any person (approximately 98%) of a defined group of healthy individuals. Applied to an individual, the recommended level is only a goal to ensure the approximately sufficient intake of a nutrient. A daily nutrient intake as recommended makes insufficient supply very unlikely. But it is not valid to conclude, on the other hand, that an intake below the recommended level implies a deficit; an intake below the recommended level only suggests the probability that the intake may be inadequate. The same applies to intakes falling below estimated values.

It is not possible to accurately assess the adequacy of nutrient intake of individuals on the basis of recommended intakes. For this purpose, it would be necessary to know the person's individual requirements. It can be estimated, however, whether the nutrient intake over an adequate period (e.g. a weekly average)

corresponds to the recommended intake and that, therefore, there is a great probability that intake is adequate. The adequacy of the nutritional status of individuals can be evaluated accurately only by including anthropometrical, biochemical and clinical dimensions.

Menu plans on the basis of reference values will satisfy individual needs only approximately. They will fail to perfectly meet an individual's requirement as the individual's requirements are not known. For individual nutrition counselling, however, reference values can serve as an orientation aid.

Planning of nutritionally adequate diets and assessing the adequacy of nutrient intakes for groups, e.g. to recognize over- or undersupply of risk groups, requires special standards as the variability among nutrient intakes in a group is greater than the variability among requirements of individual group members. The Dietary Reference Intakes (DRI) of the United States and Canada, therefore, propose a 'necessary average group intake' for reference; it has been defined as total of the average group requirement and two standard deviations of the group's nutrient intake [14, 15]. As practice has shown that nutrient intakes seldom follow normal distribution patterns and data of group requirements are rare, DGE, ÖGE, SGE and SVE continue to use reference values for planning nutritionally adequate diets for groups until more precise data are available.

Reference values, further, serve as a basis for nutritional information and education. Some of them are also used in food labelling. Reference values cannot, and do not need to be met daily, even less with each meal. It is sufficient that reference values are met within a week. Because the absorption rates of certain nutrients decrease with increasing doses, they should be ingested as regularly as possible and not in a few high doses, e.g. with fortified food at a single meal.

As different methods were used for estimating requirements and for setting recommendations and estimated values, very precise calculations should be avoided with the figures in the tables. This applies particularly to differences between consecutive age groups and between males and females. The influence of other dietary components, indulgent food and drugs or of smoking on the absorption and metabolism of certain nutrients may be greater than the difference in the figures for recommended intake between males and females or consecutive age groups.

The figures listed in the tables were calculated for the mean of the age groups and refer to the daily intake per person. Additional figures specifying daily intake per kg of body weight are only given for energy, protein and water. Body weight means not actual body weight but normal weight in relation to body size (e.g. according to the formula of Broca, or a Body Mass Index (BMI) of 24 for men and 22 for women (see table 1, page 21).

Reference values are shown in units of weight or volume (water). Of nutrients which are ingested in compounds (e.g. salts), only the proportion of nutrient in the compound may be considered (except for sodium chloride). For the vitamins A, E, niacin and folate, the auxiliary term 'equivalent' is used as the sum of the vitamin itself, metabolically active precursors, derivatives or resulting products. Reference values for the energy sources carbohydrates and fats and for essential fatty acids are shown in percent of the age- and sex-specific energy intake (guiding values) (tables 4 and 5, pages 26 and 27).

As in the EC Directive governing nutrient labelling, the following figures are used for energy values of energy-yielding nutrients: 1 g of protein = 17 kJ (4 kcal); 1 g of fat = 37 kJ (9 kcal); 1 g of carbohydrates = 17 kJ (4 kcal); 1 g of alcohol = 29 kJ (7 kcal).

The reference lists comprise reviews in books or scientific journals and also reference to special statements.

Nutrient losses

Reference values listed in the tables (part A) refer to the amounts of nutrients still present in foods as they are eaten. For some nutrients, losses occurring during cooking and other methods of pretreatment and food preparation in domestic and large institutional kitchens are described in 'Explanations' (part B). Losses caused by treatment and processing in the food trade and industry must be considered as well. Keeping foods warm causes substantial losses, e.g. of thiamin (vitamin B_1) and vitamin C (ascorbic acid). For such nutrients extra allowances must be added for losses during preparation [3]. Losses described in the explanation sections are mean values of all foods (edible portion), given customary diets and gentle preparation, including food consumed raw.

These percentage losses as well as nutrient intake calculated from nutrient tables must be considered by those planning or assessing the adequacy of nutrient supplies. The nutrient tables used should provide information about the nutrient content of the edible portion of food purchased. The edible portion corresponds to the ingestible food without taking into account waste, cooking losses and losses caused by keeping cooked food hot (e.g. nutrient tables by Souci, Fachmann, Kraut [30, 36]). Most recent data collections such as the *Bundeslebensmittelschlüssel* (German Nutrient Food Code and Data Base [BLS]) also provide information about the nutrient content of prepared food [5]. For nutritional assessment, the tables in part A are to be used, without adding allowances for losses.

The reference values do not consider household losses of edible substances. Losses such as leftovers adhering to pots and bowls, spoilage loss or other losses of edible material vary depending on the kind of food and household; they are small in some foods, e.g. egg and sugar, and larger in many foods of vegetable origin and in dietary fats. At times of short food supply, such losses are smaller than at times of sufficient and abundant food supply. With the present status of food supply in Germany, Austria and Switzerland, losses of edible substance may average 10 - 15%. In nutritional surveys (or in calculations of individual consumption) such losses are to be considered separately.

Nutrient density

Special attention should be paid to the ratio of essential nutrients to dietary energy, taking the general nutritional situation (low energy requirement due to low physical activity) into account. This problem is dealt with the concept of nutrient density, i.e. the amount of nutrients expressed per 1 Megajoule. Nutrient density values are to be regarded as guiding values which are controlled by two variables. Smaller differences in nutrient densities result from figures rounded up or down. To derive the nutrient density, guiding values for energy intake are entered as a function of the basal metabolic rate and physical activity of the different age groups and sex (children see table 4, page 26; adolescents and adults see table 5, at PAL 1.4, page 27). The calculation of nutrient densities recommended for pregnant women is based on the reference values for the age group 19 to under 25 years.

Good nutrient sources

Specially good sources of nutrients are widely accepted foods that have a nutrient density more than 3 times the density of food recommended for women over 65 years. This age group needs the highest nutrient density in view of its extremely low energy requirement.

Fortified food and food supplements

Nutrient requirements can, in principle, be satisfied by a diet composed of a wide variety of nutritious food including a high proportion of vegetable foods. There are enough conventional foods with excellent nutrient density.

Irrespective of this fact, several fortified foods for daily consumption are commercially available. Their contribution to nutrient supply cannot be specified at present because common nutrient tables do not record fortified food.

Of all fortifications only one has been shown to be necessary: fortification of table salt (sodium chloride) with iodine which is subject to legal regulation. The question of whether other food or feed needs to be fortified remains to be settled by future research.

Intolerances (e.g. lactose intolerance) or aversions to certain food, imbalanced diets, long-term or imbalanced weight reduction diets or certain diseases as well as chronic high alcohol and tobacco consumption are associated with an increased risk for inadequate supply of essential nutrients at risk. In special life situations (e.g. pregnancy, lactation, old age) the need for individual nutrients considerably increases and might not be satisfied by a balanced diet alone. In such cases, carefully selected fortified food or food supplements may be indicated. This applies, according to present knowledge, e.g. to vitamin D in elderly persons because the ability to synthesize vitamin D in the skin decreases from about the 50th year of life on [24, 28], and to vitamin B_{12}, the absorption of which is reduced in 30% of persons over 60 due to atrophic gastritis. Usually, this does not lead to megaloblastic anaemia as a sign of vitamin B_{12} deficiency, but may impair homocysteine metabolism [7, 34].

Other specific situations such as caries prevention by fluoride or vitamin D supplements for infants for rickets prophylaxis will be discussed in the chapters dealing with these nutrients. The preventive aspects of nutrients are explained in section II (page 189).

High dose nutrients for treatment of deficiencies (e.g. vitamin or iron deficiency) or other pathological conditions (e.g. absorption disorders) and for secondary prevention (e.g. vitamin E to prevent myocardial infarction) should only be taken upon medical advice and under medical supervision.

In principle, poor nutritional habits cannot be compensated for by the use of fortified food and/or food supplements. A wholesome diet provides not only essential micronutrients and macronutrients in the rights ratios; it also provides adequate amounts of dietary fibre and phytochemicals.

Undesirable effects of nutrients

Undesirable pharmacological as well as toxicological effects must be expected to occur if nutrients are ingested in quantities substantially exceeding the reference values. Ultimately, any nutrient above a certain level of intake may impair health. In this respect, the fat soluble vitamins A and D are particularly critical because they accumulate in the body and cause characteristic signs of intoxication if taken in high doses. Chemically modified nutrient derivatives, e.g. of vitamin A (retinoids), frequently have different pharmacological effects than those of

the high dose nutrient itself, including undesirable effects. Also high doses of water soluble vitamins (e.g. vitamin B_6, nicotinic acid) or of trace elements (selenium, fluoride, etc.) may have adverse effects on health. These are especially likely with self-medication with non-prescription vitamin and mineral preparations.

Thus, to avoid risks to health, it is also necessary to pay attention to the effects of nutrients in high doses. Therefore, not only recommended intakes of individual nutrients or nutrient intakes judged to be adequate are shown, but also those amounts (in terms of total daily dietary intakes, including fortified food and food supplements) for which first adverse effects have been documented with chronic intake [8, 21, 35].

The reference values ensure adequate and safe levels of intake. In general, nutrient intake is critical only when a multiple of the reference value is ingested. Anyone on a balanced diet composed of a wide variety of food according to the 10 guidelines of the German Nutrition Society will always be on the safe side [12].

Health aspects

The reference values for nutrient intake consider not only nutritive, but also health aspects in the sense of prevention of nutrition related diseases [22]. The consequences of oversupply with nutrients (detrimental in the case of energy, fat, alcohol, cholesterol, purines, sodium chloride) are as important as those of undersupply. Detailed figures are provided in the nutrition reports of the German Nutrition Society *(Deutsche Gesellschaft für Ernährung)*, of the Institute of Nutritional Sciences of the University of Vienna, and of the Federal Office of Health, Switzerland *(Bundesamt für Gesundheit, Schweiz)* as well as the National Food Consumption Survey *(Nationale Verzehrsstudie)*, Germany [4, 11, 16, 18, 19].

A glance at the cost of nutrition related diseases illustrates the economic importance of prophylaxis by a balanced health supporting diet. In the western part of the Federal Republic of Germany it was estimated at more than 80 billion DM per year for 1990 [6]. A consistent implementation of the present reference values for nutrient intake by a balanced diet and attention paid to the preventive aspects of nutrients and other food components may be of great help in preventing diseases and reducing cost (see section II, page 191).

Special life stages

Characteristics of pregnancy and lactation

For pregnancy and lactation, allowances have been added to satisfy increased needs which usually exist after the 4th month of pregnancy. Recommendations or estimated values for critical nutrients are increased from the very beginning of pregnancy as a precautionary measure. For some nutrients, different values are shown for young pregnant women (< 19 years). Otherwise, allowances are added to the reference values of the age group 19 to under 25 years.

Characteristics of the growing organism

Reference values for energy and nutrient intake during the first 4 months of life apply to breast-fed infants (for the nutrient content in human milk see table IV, page 209 according to [30]). Provided the volume of breast milk is sufficient, exclusively breast-fed infants usually grow well during the first 4 months, i.e. the baby's requirements during this period are satisfied by breast milk. After about two months, they receive a daily average of 750 ml of human milk (coefficient of variation ca. 12.5%). Infants are born with a hepatic store of certain nutrients, e.g. iron, selenium and copper. However, supplementation of vitamin D, vitamin K and fluoride during the first year of life is also advised in breast-fed infants. As the nutrient content of human milk varies and as systematic studies of infant requirements for most of the essential nutrients are not available, nutrient quantities estimated from the nutrient content of human milk only have the quality of estimated values.

Infants who are not breast-fed should be fed a commercial infant formula, if possible, during the first 4 months of life (for EC guiding values for energy and nutrient contents see table IV, page 209 [25, 26]). Nutrient quantities provided by commercial infant formulae allow for a lower bioavailability than that of human milk.

Reference values for infants apply to full term babies. Specific problems of preterm babies [31] are not addressed here. Detailed feeding instructions for preterm babies were published by the European Society of Paediatric Gastroenterology and Nutrition [13].

At the earliest at the end of the 4th month of life supplementary food should be gradually introduced because energy and nutrients supplied from human milk alone are usually no longer sufficient.

For all age groups over 4 months, reference values for energy and nutrient intake were based on the best requirement data or estimated values available in the scientific literature.

Characteristics of older people

In our society, transition from working life to retirement is defined as the point of entry into 'senior age'. From the biological point of view, however, the process of aging starts as early as after puberty. Aging is associated with a steady decrease in functional capacity. This applies to nearly every organ and cellular system. Due to substantial functional reserves the human organism is initially capable of compensating for these changes. Given an independent lifestyle and physical and mental health, furthermore, it takes a while for age-related changes to occur in an individual's nutrient supply state.

Results of recent research [7, 24, 28, 34] advise a higher intake of individual micronutrients (vitamin B_{12} and vitamin D) not before the 6th decade of life. Corresponding age-related values are shown in the respective tables. At older ages, the basal metabolic rate and also physical activity usually decrease. Energy supply should be reduced accordingly. This implies that more food of high nutrient density is needed.

In the 7th decade of life, functional losses in some organs tend to increase. Thus, septuagenarians are at greater risk for chronic and acute diseases, which often make the regular intake of different medications (multiple medication) necessary. Diseases and medication may be responsible for reduced nutrient absorption and increased nutrient turnover and/or excretion, reducing the availability of nutrients or increasing requirements. Chewing problems may be associated with the deletion of certain foods (e. g. whole-grain products) from the diet and with intentionally overcook food to soften its texture, so that preparation losses grow. In extreme cases, general nutrient intake is reduced.

People of older age are a very heterogeneous group with a variability ranging from fit and healthy to frail individuals with multiple diseases. Because of this great heterogeneity, reference values which are formulated for groups of persons, will in old age be of decreasing relevance to the individual. The physiology of old age also includes the phenomenon of diminished functional reserves, which reduces the capability of managing with nutrient quantities which slightly differ from individual needs. With increasing age, morbidity and multiple diseases with disabilities gain in importance. This makes it difficult to set reference values which are generally valid.

Aging processes, not anyway uniform in their course, are influenced by personal behaviour. This leads to individual differences in the degree of impairments of organic and metabolic functions which mainly appear with advancing age. Because of this inter-individual variability among the states of health it is desirable that the nutritional status of old people be analyzed by nutritionists to make sure guidelines are optimally adapted to the individual case. Attention should

also be paid to the psychic, social and financial situation and to the ability to buy food and prepare meals.

If the nutritional status cannot be improved by a change in diet, supplementation of essential nutrients should be advised as early as possible. Chronic nutritional failure seldom causes isolated deficiencies in individual vitamins or minerals; it is usually rather associated with an undersupply of many essential nutrients and of energy. To supplement the daily diet, a balanced liquid formula diet should be preferred to nutritional supplements which may not contain all vitamins and minerals [27].

Characteristics of popular sports

Depending on the kind, extent and intensity, popular sport activities (e.g. tennis, jogging, dancing) may require an additional up to 8.5 MJ (2000 kcal) of energy per week. In principle, it is no problem to satisfy an increased requirement for energy by conventional food on the basis of a balanced mixed diet according to the reference values presented. There is no reason to increase protein intake which would result in a higher workload for the kidneys. As carbohydrates are the most favourable source of energy, products with a high proportion of poly- and oligosaccharides should be preferred. Fluid loss by sweating should be compensated for by (mineral) water, diluted fruit juices and tea. Special isotonic drinks may do as well, but provide no essential advantages in popular sports. Additional intake of mineral and vitamin preparations is not necessary.

References

[1] Beaton, G. H.: Uses and limits of the use of the Recommended Dietary Allowances for evaluating dietary intake data. Am. J. Clin. Nutr. 41 (1985), 155-164

[2] Bässler, K.-H., Golly, I., Loew, D., Pietrzik, K.: Vitamin-Lexikon. 2. Auflage, Gustav Fischer, Stuttgart (1997)

[3] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 9 (1995), 411-416, 478-483, 551-554

[4] Bundesamt für Gesundheit (ed.): Vierter Schweizerischer Ernährungsbericht. Bern (1998)

[5] Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin (ed.): Bundeslebensmittelschlüssel II.3, Berlin (1999)

[6] Bundesministerium für Gesundheit (ed.): Ernährungsabhängige Krankheiten und ihre Kosten. Schriftenreihe des Bundesministeriums für Gesundheit, Bd. 27. Nomos Verlagsgesellschaft, Baden-Baden (1993)

[7] Carmel, R.: Cobalamin, the stomach, and aging. Am. J. Clin. Nutr. 66 (1997), 750-759

[8] Commission of the European Communities: Reports of the Scientific Committee for Food. Nutrient and energy intakes for the European Community. Thirty-first series. Office for Official Publications of the European Communities, Luxemburg (1993)

[9] Deutsche Gesellschaft für Ernährung (ed.): Empfehlungen für die Nährstoffzufuhr. 5. Überarbeitung, Umschau Verlag, Frankfurt/Main (1991)

[10] Deutsche Gesellschaft für Ernährung (ed.): Empfehlungen für die Nährstoffzufuhr der DGE, 5. Überarbeitung 1991 – Kommentar zu den Neuerungen. Ernährungs-Umschau 38 (1991), 479-483

[11] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/Main (1996)

[12] Deutsche Gesellschaft für Ernährung: Vollwertig Essen und Trinken nach den 10 Regeln der DGE. 6. Nachdruck (1999)

[13] ESPGAN Committee on Nutrition of the Preterm Infant. Wharton, B. A., Bremer, H. J., Brooks, O. G., Orzalesi, M., Putet, G., Räihä, N. C. R., Senterre, J., Shaw, J. C. L.: Nutrition and feeding of preterm infants. Blackwell Scientific Publications, Oxford (1987)

[14] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy Press, Washington D.C. (1997)

[15] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington D.C. (1998)

[16] Institut für Ernährungswissenschaften der Universität Wien (ed.); im Auftrag des Bundesministeriums für Frauenangelegenheiten und Verbraucherschutz und des Bundesministeriums für Arbeit, Soziales und Gesundheit: Österreichischer Ernährungsbericht 1998. Wien (1998)

[17] Joint FAO/WHO Expert Consultation: Requirements of Vitamin A, Iron, Folate, and Vitamin B_{12}. FAO Food and Nutrition Series No. 23, FAO, Rome 1988

[18] Kübler, W., Hüppe, R., Matiaske, B., Rosenbauer, J., Anders, H. J.: Was verzehrt der Bundesbürger? - Was sind die Folgen? Die Verbundstudie VERA und die Nationale Verzehrsstudie. Ernährungs-Umschau 37 (1990), 102-107

[19] Kübler, W., Anders, H.-J., Heeschen, W., Kohlmeier, M. (Hrsg): VERA-Schriftenreihe, Band I-XIV A (1991-1995). Wissenschaftlicher Fachverlag Dr. Fleck, Niederkleen

[20] Machlin, L. J. (ed.): Handbook of Vitamins. (Nutritional, Biochemical, and Clinical Aspects). Marcel Dekker Inc., 2nd edition, New York-Basel (1991)

[21] Mertz, W.: Trace Elements in Human and Animal Nutrition, 5th edition, Vol. I and II, Academic Press Inc., Orlando (1986)

[22] National Research Council: Diet and Health: Implications for reducing chronic disease risk. Report of the Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences. National Academy Press, Washington D.C. (1989)

[23] National Research Council: Recommended Dietary Allowances. 10th edition, National Academy of Sciences, Washington D.C. (1989)

[24] Need, A. G., Morris, H. A., Horowitz, M., Nordin, C.: Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. Am. J. Clin. Nutr. 58 (1993), 882-885

[25] Richtlinie 91/321/EWG der Kommission vom 14. Mai 1991 über Säuglingsanfangsnahrung und Folgenahrung. Abl. Nr. L 175/35-49

[26] Richtlinie 96/4/EG der Kommission vom 16. Februar 1996 zur Änderung der Richtlinie 91/321/EWG über Säuglingsanfangsnahrung und Folgenahrung. Abl. Nr. L 49/12-16

[27] Schlierf, G.: Mangelernährung geriatrischer Patienten. In: Deutsche Gesellschaft für Ernährung (ed.), Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/M. (1996), 233-250

[28] Schlierf, G., Oster, P.: Zur Vitamin-D-Zufuhr im Alter. Die Versorgungswege sind anfällig. Münch. Med. Wschr. 140 (1998), 627

[29] Shils, M. E., Olsen, J.A., Shike, M., Ross, A.C. (eds.): Modern Nutrition in Health and Disease. 9th edition, Williams & Wilkins, Baltimore (1998)

[30] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[31] Tsang, R.C., Lucas, A., Uauy, R., Zlotkin, S. (eds.): Nutritional Needs of the Preterm Infant. Scientific Basis and Practical Guidelines. Williams & Wilkins, Baltimore (1993)

[32] Tsang, R. C., Nichols, B. L. (eds.): Nutrition During Infancy. Hanley & Belfus, Philadelphia (1988)

[33] U.S. Department of Health and Human Services. The Surgeon General's Report on Nutrition and Health. Government Printing Office, Washington D.C. (1988)

[34] van Asselt, D. Z., de Groot, L. C., van Staveren, W. A., Blom, H. J., Wevers, R. A., Biemond, I., Hoefnagels, W. H.: Role of cobalamin intake and atrophic gastritis in mild cobalamin deficiency in older Dutch subjects. Am. J. Clin. Nutr. 68 (1998), 328-334

[35] Walter, P., Brubacher, G., Stähelin, H. (eds.): Elevated dosages of vitamins; Benefits and hazards. H. Huber, Toronto-Bern-Stuttgart (1989)

[36] Wirths, W.: Kleine Nährwerttabelle der DGE. 41. Auflage, Umschau Braus, Heidelberg (1999)

[37] Yates, A. A., Schlicker, S. A., Suitor, C. W.: Dietary Reference Intakes: the new basis for recommendations for calcium and related nutrients, B vitamins, and choline. J. Am. Diet. Assoc 98 (1998), 699-706

Energy

Energy requirement is calculated by considering the basal metabolic rate, physical activity (muscle work), thermogenesis after food intake and the needs for growth, pregnancy and lactation. The recommended level of energy supply is shown in megajoules (MJ) and kilocalories (kcal) (1 MJ = 239 kcal; 1 kcal = 4184 kJ = 0.004184 MJ).

Given the usual physical load of ordinary day-to-day activities, the basal metabolic rate (BMR) stands for the major part of energy consumption. Its level is closely correlated to lean body mass which decreases with age. In men, because of their greater lean body mass, the basal metabolic rate is about 10% higher than in women.

The basal metabolic rate can either be calculated or determined by means of calorimetry. To calculate the basal metabolic rate, several predictive formulae are available which are derived either from the lean body mass, body fat content and age and sex [14] or (more simply) from body weight (if necessary also from body height) and age and sex [5, 16]. The coefficient of variation for the basal metabolic rate calculated according to the predictive formulae is about 8%. The basal metabolic rate is determined more precisely (± 3%) by indirect calorimetry via measurement of oxygen consumption and carbon dioxide production. Determination only from oxygen consumption is less expensive and still sufficiently precise.

Table 1 contains reference values for body height and body weight for infants, children, adolescents and adults of both sexes. Reference values pertaining to body weight of adults have been calculated from representative data of body height by means of the formula of the Body Mass Index (BMI). For smaller or larger individuals, values have to be modified by using the BMI formula (table 1, footnote 3).

Table 2 provides some examples of the basal metabolic rate (calculated according to WHO [16]) on the basis of the guiding values in table 1. Determination or calculation of the basal metabolic rate is gaining in importance because daily energy requirements are now usually defined on the basis of the basal metabolic rate: energy requirement is indicated in multiples of the basal metabolic rate as a function of physical work and other activities. Thermogenesis after food intake is of less importance in terms of quantity. 8 - 10% of the energy supplied from a usual mixed diet composed of vegetable and animal foods is needed for uptake and storage of the ingested nutrients. This is associated with increased heat production called dietary induced thermogenesis (DIT) [11].

A substantial part of dietary energy is spent on physical activity. According to common international practice, energy expenditure is shown in multiples of the basal metabolic rate (BMR), and not in terms of absolute values (MJ or kcal).

Table 1: Reference data of body height and body weight for calculation of the basal metabolic rate (BMR)

Age	Body height (cm)		Body weight (kg)	
	m	f	m	f
Infants[1]				
0 to under 4 months	57.9	56.5	5.1	4.7
4 to under 12 months	70.8	68.9	8.7	8.1
Children[1]				
1 to under 4 years	90.9	90.5	13.5	13.0
4 to under 7 years	113.0	111.5	19.7	18.6
7 to under 10 years	129.6	129.3	26.7	26.7
10 to under 13 years	146.5	148.2	37.5	39.2
13 to under 15 years	163.1	160.4	50.8	50.3
Adolescents and adults[2]				
15 to under 19 years[3]	174.0	166.0	67.0	58.0
19 to under 25 years[4]	176.0	165.0	74.0	60.0
25 to under 51 years[4]	176.0[5]	164.0[5]	74.0	59.0
51 to under 65 years[4]	173.0	161.0[5]	72.0	57.0
65 years and older[4]	169.0	158.0[5]	68.0	55.0

[1] Reference values correspond to the 50th percentiles of growth for dates of the US National Center for Health Statistics (NCHS) which were used also in the RDA [8] as reference values. Values are interpolated for the values halfway between the range limits, i.e. for 2.0, 8.0 months and 2.5, 5.5, 8.5, 11.5, 14.0 years

[2] According to height measurements in a group of persons representative of the Federal Republic of Germany (Pudel V: Ernährungsbericht 1980 [3]), and unpublished data of the Cooperative Study: Nutrition Survey and Risk Factor Analysis (VERA) and the National Food Consumption Survey (NVS)

[3] Body weight calculated from height measurements based on a desirable Body Mass Index (BMI = body weight [kg]/squared body height [m^2] of 22 for men and 21 for woman [12]

[4] BMI 24 for men and 22 for women (definition of BMI see 3)

[5] According to height measurements of the Health Survey East-West (*Gesundheitssurvey Ost-West, Befragungs- und Untersuchungssurvey in den neuen und alten Bundesländern)*, Public Use File OW91 (1990 - 1992), documentation of the data set compiled by Dr. Heribert Stolzenberg, Robert Koch Institute, Institute for Communicable and Non-communicable Diseases, Berlin, October 1995

The average total energy expenditure (TEE) of an individual can be measured by the doubly labelled water method (DLW) while the individual's basal metabolic rate (BMR) can be determined by indirect calorimetry (or calculated by predictive formulae). Average total energy requirement, in multiples of BMR, equals the quotient TEE/BMR which depends upon occupational activity and leisure time behaviour. This value is called 'physical activity level' (PAL) [6]. In a normal life situation it may vary between 1.2 and 2.4 [13]. In more than 500 measurements in working adults with predominantly sedentary activity PAL averaged 1.55 - 1.65 [1]. In view of usually low physical activity and frequent overweight, a lower PAL (1.4) should be used for the guiding value of energy intake in the individual case (table 5).

The advantage of this procedure is that, by referring to the BMR, factors influencing energy requirement such as body weight, age and sex are *a priori* taken into account. Thus, energy expenditure for defined physical activities is directly comparable among different individuals. Factors for lying, standing, walking and for occupational and leisure activities of different kinds can be taken from corresponding tables [e.g. 6, 16] (see also table 3). Daily energy requirement results from the amount of time spent on these activities. Assuming e.g. for a housewife 8 hours of work with a high average energy expenditure of 2.4 x BMR and 8 hours of activities with a medium energy expenditure of 1.6 x BMR as well as 8 hours of sleep at 0.95 x BMR, the mean daily energy requirement is (2.4 x 8 + 1.6 x 8 + 0.95 x 8)/24 = 1.65 x BMR.

Table 2: Basal metabolic rate, calculated using the reference data of table 1 and the predictive formula of FAO/WHO/UNU [16] (based on sex, age and body weight)

Age	Body weight (kg)		Base metabolic rate (MJ/day)		Base metabolic rate (kcal/day)	
	m	f	m	f	m	f
15 to under 19 years	67	58	7.6	6.1	1820	1460
19 to under 25 years	74	60	7.6	5.8	1820	1390
25 to under 51 years	74	59	7.3	5.6	1740	1340
51 to under 65 years	72	57	6.6	5.3	1580	1270
65 years and older	68	55	5.9	4.9	1410	1170

The new methodology of measuring energy expenditure by means of doubly (stable) labelled water enables a more precise determination of daily TEE than the indirect calorimetry used so far; it also complies with international standards [12]. The results obtained are not comparable to earlier figures; representing a direct and continuous measurement of all daily energy expenditures, they are, in

fact, higher than before. The results in table 4 refer to persons of normal weight and with corresponding physical activity.

Table 3 shows some examples of experimental average daily energy expenditures (by DLW or indirect calorimetry) for different occupational and leisure activities.

As a consequence of labour-saving mechanization and automation of the work place, occupational energy needs have declined. The grouping of occupational activities into categories ranging from light to heavy work has to be revised. Occupations once associated with heavy work have now to be grouped with occupations requiring less energy.

Many employed persons with mainly sedentary activities have been found to spend more energy during leisure time than in their job. For sports or other strenuous leisure time activities (30 - 60 minutes, 4 - 5 times a week) 0.3 PAL per day may be added to the daily energy expenditure (table 3).

Table 3: Examples of the average daily total energy expenditure in different occupational and leisure activities of adults

Occupational and leisure activities	**PAL**[1,2]	**Examples**
at rest, exclusively sedentary or lying	1.2	old, infirm individuals
exclusively sedentary activity, little or no strenuous leisure activity	1.4-1.5	office employees, precision mechanics
sedentary activity, also additional energy requirements for occasional walking and standing[2]	1.6-1.7	laboratory assistants, drivers, students, assembly line workers
predominantly standing or walking work[2]	1.8-1.9	housewives, salespersons, waiters, mechanics, traders
heavy occupational work[2]	2.0-2.4	construction workers, farmers, forest workers, miners, high-performance athletes

1 PAL = (physical activity level), average daily energy requirement for physical activity as a multiple of the basal metabolic rate

2 For sports or strenuous leisure activities (30-60 minutes, 4-5 times a week) 0.3 PAL units per day may be added

In setting guiding values for energy intake during growth, additional energy needed for the development of body mass must be allowed for. Prolonged under- or oversupply of energy will put young people's health at risk.

The guiding values given in table 4 for the (average) energy intake in children of different age groups apply to moderate physical activity and to body height and body weight according to the respective 50th percentile (median) of the reference values (table 1). The guiding values for energy [2,15] correspond to recent proposals by FAO/WHO/UNU experts [16]. They are based on experimental data for total energy expenditure in the different age groups. Total energy expenditure has been determined by means of doubly (stable) labelled water (DLW) and heart rate monitoring. From energy expenditure data for children with moderate physical activity, guiding values were estimated for relatively inactive children (-2 SD or -12%) and for physically very active children (+2 SD or +12%) [15].

In term babies, mean energy expenditure doubles from about 230 ± 59 kJ/kg/day (55 ± 14 kcal/kg/day) during the 1st week of life to about 460 kJ/kg/day (110 kcal/kg/day) at the end of the 3rd week of life. This is the time when the infant's growth rate reaches a maximum (more than 2 cm of body length/month). After the 3rd month, the growth rate slows down and the energy requirement related to body weight decreases.

If a child is larger or smaller than the age- and sex-related 50th percentile of body height but has normal weight for its height, its energy requirement corresponds to that of children of the age at which the 50th percentile of body height agrees with the actual body height of this child. It could be helpful in the individual case to resort to the original data for the age related 50th percentile of body height in the individual years of life [4]. If there is over- or underweight, corrections must be made by using the body weight-related reference values for energy requirement (table 4).

Summarizing evaluations of a great many studies in which energy requirement of adults and of older people from developed countries have been determined by the doubly labelled water method suggest that energy requirement must be estimated higher than before [1, 10, 13]. This particularly applies to the energy needs of men of all age groups. The energy needs of women must be estimated higher as well, but not as much as for men. The guiding values for energy intake in table 4 take this development into account.

It should be noted that the reference values in table 4 refer to persons of 'normal weight' and with desirable physical activity; in the presence of over- or underweight, corrections are necessary in order to reach or maintain normal weight. In the individual case, actual energy requirement, i.e. correct energy intake, can be estimated only from regular monitoring of body weight.

Table 5 contains guiding values for energy intake in adolescents and adults of different age as a function of the basal metabolic rate and different physical activity levels (PAL values, see table 3). The range of PALs, strictly speaking, may vary from 1.2 for exclusively sedentary lifestyle to 2.4 for heavy labourers [13]. Here, each individual must be classified properly. In order to reduce the risks of obesity, cancer and myocardial infarction, a PAL of at least 1.75 is considered necessary (table 4) [1, 12].

Men and women over 65 years are a particularly heterogeneous group in their energy requirements. On the one hand there are subjects whose physical activity is comparable to that of younger persons, on the other hand there are people whose mobility is clearly restricted [10]. Therefore, great deviations in actual individual energy expenditure may occur.

For the total duration of pregnancy most recent studies have shown that an additional 300 MJ (71,700 kcal) are needed [9]. It is recommended that this requirement should be met evenly over the whole period by an additional intake of 1.1 MJ/day (255 kcal/day) [9] (table 5).

For breast-feeding mothers an additional energy intake of 2.7 MJ/day (635 kcal/day) is recommended for the first 4 months post partum. After the 4^{th} month additional energy intake depends on whether the mothers continue breast-feeding fully or partly. Fully breast-feeding mothers then need an additional 2.2 MJ/day (525 kcal/day), partly breast-feeding mothers only 1.2 MJ/day (285 kcal/day) [9]. If physical activity during pregnancy or lactation changes considerably, compared to the non-pregnant and non-lactating state, energy intake must be corrected by the energy amount resulting from the product BMR x PAL (table 5).

As a reference measure for adults, the Body Mass Index (BMI: weight in kilograms divided by height in metres squared) has been introduced. Given a body weight of 68 kg and a body height of 1.76 m, BMI equals 22 which is within the normal range. The normal range for both men and women is BMI 20 to BMI 25 kg/m^2. Prolonged energy intake exceeding energy expenditure leads to obesity with adverse consequences for health [7].

Recent epidemiological findings support the assumption that the risk for obesity is influenced not only by the mass of adipose tissue, but also by its distribution [17]. A disposition to adipose tissue deposits in the abdomen (masculine or android form) is more frequently associated with cardiovascular risk factors than a disposition to adipose tissue at the hips (feminine or gynoid form). However, women may also have an android fat distribution and men, vice versa, a gynoid. Adipose tissue distribution can be roughly determined by the waist to hip (W/H) ratio. Values above 1.0 in men and above 0.8 in women suggest that the person is at additional cardiovascular risk.

Table 4: Guiding values for average energy intake[1] in MJ and kcal/day in individuals with BMI in the normal range and corresponding physical activity in kJ and kcal/kg body weight (see footnote[2]). In cases of deviations from the normal range, especially in overweight individuals and low physical activity, the guiding values need to be corrected. Actual body weight is the controlling parameter.

Age	MJ/day		kcal/day		Values for moderate physical activity kJ/kg		Values for moderate physical activity kcal/kg		Values for low/high physical activity kcal/kg	
	m	f	m	f	m	f	m	f	m	f
Infants[3]										
0 to under 4 months	2.0	1.9	500	450	390	380	94	91		
4 to under 12 months	3.0	2.9	700	700	380	380	90	91		
Children[4]										
1 to under 4 years	4.7	4.4	1100	1000	380	370	91	88	83 / [5]	80 / [5]
4 to under 7 years	6.4	5.8	1500	1400	340	330	82	78	74 / [5]	70 / [5]
7 to under 10 years	7.9	7.1	1900	1700	310	280	75	68	66 / 83	60 / 76
10 to under 13 years	9.4	8.5	2300	2000	270	230	64	55	56 / 71	49 / 62
13 to under 15 years	11.2	9.4	2700	2200	230	200	56	47	50 / 63	41 / 52
Adolescents and adults[2]										
15 to under 19 years	13.0	10.5	3100	2500	195	180	46	43	39 / 60	36 / 55
19 to under 25 years	12.5	10.0	3000	2400	170	165	41	40	35 / 54	33 / 51
25 to under 51 years	12.0	9.5	2900	2300	165	165	39	39	34 / 52	33 / 50
51 to under 65 years	10.5	8.5	2500	2000	145	145	35	35	32 / 48	32 / 48
65 years and older	9.5	7.5	2300	1800	140	135	34	33	30 / 46	30 / 46

[1] Data in tables 1 and 2 were taken into account

[2] Basal metabolic rates for persons of normal weight in table 2 were multiplied by factors (PALs) which characterize the groups' age-adjusted habitual physical activity. The average daily energy requirement of these groups thus obtained is taken as guiding value. In accordance with [1] and the report of the Scientific Committee for Food, Commission of the European Communities [12], the following PALs were used for both sexes: 1.75 for persons of 15 to under 25 years; 1.70 for persons of 25 to under 51 years; 1.60 for persons of 51 to 65 years and older. The data in column 6 for low/high levels of physical activity were based on PALs of 1.45 and 2.2 (see table 3, mean values)

[3] 0 to under 12 months: non-breast-fed infants, according to [2], mean values of the age group (breast-fed infants: 0 to under 4 months: boys 368 kJ/kg (88 kcal/kg); girls 356 kJ/kg (85 kcal/kg); 4 to under 12 months: boys 347 kJ/kg (83 kcal/kg); girls 351 kJ/kg (84 kcal/kg)

[4] 1 to under 15 years, mean values of the age group (moderate physical activity), for 'low physical activity levels' 12% (corresponding to two standard deviations) were deducted, for 'high physical activity levels' 12% were added [15]

[5] No measurements

Table 5: Guiding values for average energy intake in persons of different age as a function of the basal metabolic rate and increasing physical activity (for PAL values see table 3). In cases of deviations from the normal range, especially in overweight individuals and low physical activity, the guiding values need to be adjusted. Actual body weight is the controlling parameter.

Age	Basal metabolic rate		Physical activity (PAL)							
			1.4		1.6		1.8		2.0	
	MJ/day	kcal/day	MJ	kcal	MJ	kcal	MJ	kcal	MJ	kcal
Adolescents and adults (m)										
15 to under 19 years	7.6	1820	10.6	2500	12.2	2900	13.7	3300	15.2	3600
19 to under 25 years	7.6	1820	10.6	2500	12.2	2900	13.7	3300	15.2	3600
25 to under 51 years	7.3	1740	10.2	2400	11.7	2800	13.1	3100	14.6	3500
51 to under 65 years	6.6	1580	9.2	2200	10.6	2500	11.9	2800	13.2	3200
65 years and older	5.9	1410	8.3	2000	9.4	2300	10.6	2500	11.8	2800
Adolescents and adults (f)										
15 to under 19 years	6.1	1460	8.5	2000	9.8	2300	11.0	2600	12.2	2900
19 to under 25 years[1,2]	5.8	1390	8.1	1900	9.3	2200	10.4	2500	11.6	2800
25 to under 51 years[1,2]	5.6	1340	7.8	1900	9.0	2100	10.1	2400	11.2	2700
51 to under 65 years	5.3	1270	7.4	1800	8.5	2000	9.5	2300	10.6	2500
65 years and older	4.9	1170	6.9	1600	7.5	1800	8.8	2100	9.8	2300

[1] **Pregnant women** receive an additional 1.1 MJ/day (255 kcal/day) for the duration of pregnancy (according to Prentice [9]); the allowance is independent of the respective PAL.

[2] **Breast-feeding mothers** receive the following allowances (according to Prentice [9]); allowances are independent of the respective PAL:
– up to completion of the 4th month: + 2.7 MJ/day (635 kcal/day)
– continued full breast-feeding after the 4th month: + 2.2 MJ/day (525 kcal/day)
– partial breast-feeding after the 4th month: + 1.2 MJ/day (285 kcal/day)

References

[1] Black, A. E., Coward, W. A., Cole, T. J., Prentice, A. M.: Human energy expenditure in affluent societies: an analysis of 574 doubly-labelled water measurements. Eur. J. Clin. Nutr. 50 (1996), 72-92

[2] Butte, N. F.: Energy requirements of infants. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S24-S36

[3] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1980. Druckerei Henrich, Frankfurt/Main (1980)

[4] Hamill, P. V., Drizd, T. A., Johnson, C. L., Reed, R. B., Roche, A. F., Moore, W. M.: Physical growth: National Center for Health Statistic percentiles. Am. J. Clin. Nutr. 32 (1979), 607-629

[5] Harris, J. A., Benedict, F. G.: A Biometric Study of Basal Metabolism in Man. Carnegie Institution of Washington. Publ. No. 279, Washington D.C. (1919)

[6] James, W. P. T., Schofield, E. C.: Human Energy Requirements - A Manual for Planners and Nutritionists. Oxford University Press (1990)

[7] National Institutes of Health (NIH): Consensus Development Panel on the Health Implications of Obesity: Health Implications of Obesity. Ann. Intern. Med. 103 (1985), 1073-1077

[8] National Research Council: Recommended Dietary Allowances. 10th edition, National Academy of Sciences, Washington D.C. (1989)

[9] Prentice, A. M., Spaaij, C. J., Goldberg, G. R., Poppitt, S. D., van Raaij, J. M., Totton, M., Swann, D., Black, A. E.: Energy requirements of pregnant and lactating women. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S82-S111

[10] Roberts, S. B.: Energy requirements of older individuals. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S112-S118

[11] Robinson, S. M., Jaccard, C., Persaud, C., Jackson, A. A., Jequier, E., Schutz, Y.: Protein turnover and thermogenesis in response to high-protein and high-carbohydrate feeding in men. Am. J. Clin. Nutr. 52 (1990), 72-80

[12] Scientific Committee for Food (SCF), Commission of the European Communities: Nutrient and Energy Intakes for the European Community, Office for the Official Publications of the European Communities, Luxembourg (1993)

[13] Shetty, P. S., Henry, C. J., Black, A. E., Prentice, A. M.: Energy requirements of adults: an update on basal metabolic rates (BMRs) and physical activity levels (PALs). Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S11-S23

[14] Tataranni, P. A., Ravussin, E.: Variability in metabolic rate: biological sites of regulation. Int. J. Obes. Relat. Metab. Disord. Suppl. 19/4 (1995), 102-106

[15] Torun, B., Davies, P. S., Livingstone, M. B., Paolisso, M., Sackett, R., Spurr, G. B.: Energy requirements and dietary energy recommendations for children and adolescents 1 to 18 years old. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S37-S81

[16] WHO (World Health Organization): Energy and protein requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. WHO Technical Report Series 724, Geneva (1985)

[17] Wolfram, G.: Fettsucht: Neubewertung des Risikos. Ernährungs-Umschau 37 (1990), 347-354

Organic components

Organic components, primarily protein, fat, carbohydrates and alcohol, are supplied from food in daily amounts of up to several hundred grams. Only some of their constituents, e.g. certain amino acids or fatty acids, are essential, the majority of constituents serves as an energy source.

Protein

A. Recommended intake

Age	Protein					
	g/kg[1]/day		g/day		g/MJ[2] (Nutrient density)	
	m	f	m	f	m	f
Infants						
0 to under 1 month	2.7		12	12	6.0	6.3
1 to under 2 months	2.0		10	10	5.0	5.3
2 to under 4 months	1.5		10	10	5.0	5.3
4 to under 6 months	1.3		10	10	3.3	3.4
6 to under 12 months	1.1		10	10	3.3	3.4
Children						
1 to under 4 years	1.0		14	13	3.0	3.0
4 to under 7 years	0.9		18	17	2.8	2.9
7 to under 10 years	0.9		24	24	3.0	3.4
10 to under 13 years	0.9		34	35	3.6	4.1
13 to under 15 years	0.9		46	45	4.1	4.8
Adolescents and adults						
15 to under 19 years	0.9	0.8	60	46	5.7	5.4
19 to under 25 years	0.8		59	48	5.6	5.9
25 to under 51 years	0.8		59	47	5.8	6.0
51 to under 65 years	0.8		58	46	6.3	6.2
65 years and older	0.8		54	44	6.5	6.4
Pregnant women from the 4th month				58		6.3
Lactating women[3]				63		5.8

[1] Related to reference weight

[2] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[3] About 2 g of additional protein intake per 100 g of secreted milk

B. Explanations

Dietary protein provides the body with amino acids and other nitrogenous compounds needed to synthesize endogenous proteins and other metabolically active substances. Only for amino acids is there a biochemically based requirement. But recommendations have still been formulated for protein, as in healthy humans amino acids are exclusively provided from this source.

The nine amino acids indispensable (formerly "essential") for adult humans are histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine which have to be supplied from the diet. Whether cysteine and tyrosine can partly replace methionine and phenylalanine (respectively) is still under discussion. In seven of the indispensable amino acids, the carbon skeletons of the corresponding keto acids are indispensable. Lysine and threonine, however, cannot be synthesized from the corresponding keto acids by transamination. Several studies have shown that a histidine-deficient diet observed over a prolonged period reduces plasma histidine concentration and restricts haemoglobin synthesis [26, 27]. Hence histidine is also considered nutritionally indispensable. Dispensable (previously: non-essential) amino acids, however, are needed as well to ensure adequate growth and to maintain body protein equilibrium (nitrogen balance) [25, 33, 39]. Therefore, a balanced diet must contain adequate amounts of both indispensable amino acids and proteins.

In adults, the experimentally determined average requirement for high-quality protein (egg, milk, meat, fish; true digestibility ≥ 95%) amounts to 0.6 g of protein per kg body weight per day [37]. With individual variability included, this value increases to 0.75 g of protein per kg body weight per day. Allowing for a frequently reduced protein digestibility in a mixed diet, 0.8 g of protein per kg body weight per day are recommended. Thus, dietary protein from a balanced mixed diet accounts for 8 – 10% of the dietary energy in adults. Lacto- and ovolactovegetarians (mixed diet based on vegetable protein sources plus milk and eggs) are adequately supplied with indispensable amino acids, provided the protein intake is as recommended and energy requirement is adequately met. Adults on a strictly vegan diet have to plan their menus carefully to make sure that their requirements for nutritionally indispensable amino acids are met. In small children it is generally impossible to satisfy this requirement from vegan diets.

Adult requirement for amino acids is at present the object of scientific discussion [36, 38]. There is a lack of satisfactory data needed to revise amino acid requirement values for adults. Thus, as an interim solution, it has been recommended to assess the capability of dietary proteins to meet indispensable amino acid requirements by comparing their amino acid pattern (mg amino acids/g dietary protein) with the amino acid requirement pattern (mg amino acids/g recommended protein intake) for 2- to 5-year-old preschool children and to correct the

score by the true protein digestibility (protein-digestibility corrected amino acid score, PDCAAS [14, 15]). The PDCAAS applies to all children over 2 years of age and to adults. The PDCAAS, by definition, relates to the first limiting amino acid; values below 1 are indicative of insufficient supply. For example the first limiting amino acid in wheat is lysine; its PDCAAS is below 0.5. This means that, if protein requirement is exclusively met by wheat protein, the requirement for lysine would not be met. Vegans, and especially those who live on cereal products exclusively, are thus of risk for lysine deficiency if their diet does not contain high-lysine plant proteins (pulses) in sufficient quantity. Assessing protein quality for human nutrition on the basis of what is needed by 2- to 5-year-old children is a pragmatic interim solution [15]. It may be used as long as satisfactory data allowing a re-assessment of amino acid requirements of individuals over 2 years of age are not available.

Some experimental data give reason to assume that older individuals (65 years and older) need more protein than younger adults [8]. However, as the number of available studies directly comparing younger and older adults is still insufficient, a protein intake of 0.8 g per kg body weight per day remains the recommendation for elderly persons.

Protein requirement has been found not to increase with increased physical activity [13, 32]. Several studies have shown that additional protein intake in excess of the (age related) recommendation (total intake 2.5 g of protein per kg body weight per day) neither influences the whole body protein turnover rate and lean body mass nor increases muscle mass or strength, even in the case of very intensive physical training [9, 21, 28, 32]. Adults practising light and moderate sports can be sure of an adequate protein supply if their energy needs are met and protein intake is in line with that determined in national surveys (e.g. *Nationale Verzehrsstudie* [10]).

Protein requirement of the growing organism is defined by the need for maintenance and growth [11]. The share of protein required for growth decreases from about 60% during the first month of life down to 11% between the ages of 2 - 5 years. The rapid change in protein requirement during the first months is the reason for subdivision of the recommended protein intake during the first year of life [11]. As fully breast-fed infants grow well during the first 6 months, their protein supply from human milk is taken as the basis for protein requirement during the first 6 months of life [11].

Protein requirement of infants between 6 and 12 months is calculated using a factorial method derived from nitrogen balance experiments. Maintenance requirement is estimated at 0.56 g of protein per kg body weight per day. Interindividual variability of maintenance and growth requirements is taken into account by an age-dependent allowance between 35% and 31% for body protein increase [11].

The recommendation derived applies to high-quality protein (e.g. milk protein). After the 2nd month of life the amount now recommended is smaller than in earlier recommendations. The large requirement during the first two months of life is fully taken into account.

3 - 4 months post partum, protein accounts for about 8% (4.8 g/MJ = 2 g/100 kcal) of the energy content in breast milk, assuming a crude protein content (total nitrogen x 6.25) of about 10 g/l and a gross energy content of 2.9 MJ/l (690 kcal/l). The recommended nutrient density for infants who are not exclusively breast-fed therefore is 4.8 g of protein/MJ (2 g/100 kcal) during the first 2 months of life, then 4 g protein/MJ (1.65 g/100 kcal) up to the 6th month and 3.5 g of protein/MJ (1.46 g/100 kcal) up to the 12th month. In infants fed infant formulae with a protein-energy ratio of 4.1 g/MJ (1.7 g/100 kcal), similar growth data and similar concentrations of plasma urea, plasma amino acids and plasma albumin have been found as in breast-fed infants [17, 18]. To avoid the risk of excessive renal stress and dehydration, the protein-energy ratio should remain below 7.6 g/MJ (3.2 g/100 kcal) [41].

The protein requirement of children and adolescents has been determined in the same way as the factorial method for older infants over 6 months [11]. The requirement includes a value for maintenance and for growth. A re-evaluation of available studies on protein requirement in children and adolescents has shown a maintenance requirement of 0.63 g of protein per kg body weight per day [11]. The requirement for growth declines as a function of age; thus total protein requirement ranges accordingly from 0.7 to 0.63 g per kg body weight per day. By adding a 30% allowance for individual variability in protein utilization and digestibility one obtains the recommended weight-related protein intake. The share of dietary protein in the total energy intake in children under 4 years of age has been estimated at 8% and in children between 4 and 13 years at 10% [35]. This is considerably less than 14% which the *Nationale Verzehrsstudie* has shown in adults [10].

During pregnancy, protein need starts to increase from the 4th month. From this time an additional 10 g of protein per day is necessary. The recommended protein intake for lactating women is derived from the amount of protein secreted in the milk. It amounts to a mean of 7 - 9 g per day [2, 22]. Given a 70% protein utilization and allowing for two standard deviations, an additional 15 g of protein per day are required [37].

So far, experiments have revealed no adverse effect of protein intake in excess of the recommended amount. Nor has an excessive protein intake been shown to produce any positive physiological effects, however [31]. With increasing protein intake the amount of protein metabolites which have to be excreted increase as well; this is accompanied by an increase in the renal glomerular filtration rate

[6] and in renal calcium excretion [4, 24, 40] which may have negative effects on calcium balance and bone health [5, 16] and involves a risk of calcium oxalate stones forming in the kidneys [23]. Increasing protein intake, furthermore, leads to a moderate metabolic acidosis [4, 20] with potentially negative but not precisely known negative consequences for the maintenance of skeletal muscle mass [3]. Indications of a relation between protein intake and insulin resistance have been reported as well [29, 34].

Attention must also be paid to the fact that the intake of animal protein is generally associated with a concurrent intake of fat, cholesterol and - except for egg and milk protein - of purines. Protein intakes of > 2 g per kg of body weight per day lead to reduced plasma concentrations of certain amino acids [19, 30] otherwise only observed under catabolic stress [1, 7].

As long as definitive data on negative effects of protein intakes far above the recommended values are not available, it seems advisable for safety reasons to set the upper limit of protein intake at 2.0 g of protein per kg of body weight per day for adults [12], corresponding to an average daily protein intake of 120 g for women and 140 g for men.

References

[1] Abcouwer, S. F., Lohmann, R., Bode, B. P., Lustig, R. J., Souba, W. W.: Induction of glutamine synthetase expression after major burn injury is tissue specific and temporally variable. J. Trauma 42 (1997), 421-428

[2] Allen, J. C., Keller, R. P., Archer, P., Neville, M. C.. Studies in human lactation: milk composition and daily secretion rates of macronutrients in the first year of lactation. Am. J. Clin. Nutr. 54 (1991), 69-80

[3] Bailey, J. L.: Metabolic acidosis and protein catabolism: mechanisms and clinical applications. Miner. Electrolyte Metab. 24 (1998), 13-19

[4] Ball, D., Maughan, R. J.: Blood and urine acid-base status of premenopausal omnivorous and vegetarian women. Br. J. Nutr. 78 (1997), 683-693

[5] Barzel, U. S., Massey, L. K.: Excess dietary protein can adversely affect bone. J. Nutr. 128 (1998), 1051-1053

[6] Brändle, E., Sieberth, H. G., Hautmann, R. E.: Effect of chronic protein intake on the renal function in healthy subjects. Eur. J. Clin. Nutr. 50 (1996), 734-740

[7] Calder, P. C.: Fuel utilization by cells of the immune system. Proc. Nutr. Soc. 54 (1995), 65-82

[8] Campbell, W. W., Evans, W. J.: Protein requirements of elderly people. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S180-S185

[9] Carraro, F., Hartl, W. H., Stuart, C. A., Layman, D. K., Jahoor, F., Wolfe, R. R.: Whole body and plasma protein synthesis in exercise and recovery in human subjects. Am. J. Physiol. 258 (1990), E821-E831

[10] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/Main (1996), 40-41

[11] Dewey, K. G., Beaton, G., Fjeld, C., Lönnerdal, B., Reeds, P. J.: Protein requirement for infants and children. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S119-S150

[12] Durnin, J. V., Garlick, P., Jackson, A. A., Schürch, B., Shetty, P. S., Waterlow, J. C.: Report of the IDECG Working Group on lower limits of energy and protein and upper limits of protein intakes. International Dietary Energy Consultative Group. Eur. J. Clin. Nutr. 53 (Suppl 1) (1999), S174-S176

[13] El-Khoury, A. E., Forslund, A., Olsson, R., Branth, S., Sjödin, A., Andersson, A., Atkinson, A., Selvaraj, A., Hambraeus, L., Young, V. R.: Moderate exercise at energy balance does not affect 24-h leucine oxidation or nitrogen retention in healthy men. Am. J. Physiol. 273 (1997), E394-E407

[14] Erbersdobler, H.: Ein neues System zur Proteinbewertung. Der Protein Digestibility Corrected Amino Acid Score (PDCAAS). Ernährungs-Umschau 39 (1992), 243-247

[15] FAO (Food and Agriculture Organization of the United Nations): Protein quality evaluation. Report of the Joint FAO/WHO Expert Consultation, Bethesda, MD, USA, FAO Food and Nutrition Paper No. 51, Rome (1991)

[16] Feskanich, D., Willett, W. C., Stampfer, M. J., Colditz, G. A.: Protein consumption and bone fractures in women. Am. J. Epidemiol. 143 (1996), 472-479

[17] Fomon, S. J., Ziegler, E. E., Nelson, S. E., Frantz, J. A.: What is the safe protein-energy ratio for infant formulas? Am. J. Clin. Nutr. 62 (1995), 358-63

[18] Fomon, S. J., Ziegler, E. E., Nelson, S. E., Rogers, R. R., Frantz, J. A.: Infant formula with protein-energy ratio of 1.7 g/100 kcal is adequate but may not be safe. J. Pediatr. Gastroenterol. Nutr. 28 (1999), 495-501

[19] Forslund, A. H., Hambraeus, L., van Beurden, H., Holmbäck, U., El-Khoury, A. E., Hjorth, G., Olsson, R., Stridsberg, M., Wide, L., Akerfeldt, T., Regan, M. M., Young, V. R.: Inverse relationship between protein intake and plasma free amino acids in healthy men, at physical exercise. Am. J. Physiol. Endocrinol. Metab. 278 (2000), E857-867

[20] Frassetto, L. A., Todd, K. M., Morris, R. C. Jr., Sebastian, A.: Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. Am. J. Clin. Nutr. 68 (1998), 576-83

[21] Garlick, P. J., McNurlan, Patlak, C. S.: Adaptation of protein metabolism in relation to limits to high dietary protein intake. Eur. J. Clin. Nutr. 53 (Suppl 1) (1999), S34-S43

[22] Heinig, M. J., Nommsen, L. A., Peerson, J. M., Lonnerdal, B., Dewey, K. G.: Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: the DARLING Study. Am. J. Clin. Nutr. 58 (1993), 152-161

[23] Holmes, R. P., Goodman, H. O., Hart, L. J., Assimos, D. G.: Relationship of protein intake to urinary oxalate and glycolate excretion. Kidney Int. 44 (1993), 366-372

[24] Itoh, R., Nishiyama, N., Suyama, Y.: Dietary protein intake and urinary excretion of calcium: a cross-sectional study in healthy Japanese population. Am. J. Clin. Nutr. 67 (1998), 438-444

[25] Kies, C.: Comparative value of various sources of nonspecific nitrogen for the human. J. Agric. Food Chem. 22 (1974), 190-193

[26] Kopple, J. D., Swendseid, M. E.: Effect of histidine intake on plasma and urine histidine levels, nitrogen balance and N tau-methylhistidine excretion in normal and chronically uremic men. J. Nutr. 111 (1981), 931-942

[27] Kopple, J. D., Swendseid, M. E.: Evidence that histidine is an essential amino acid in normal and chronically uremic man. J. Clin. Invest. 55 (1975), 881-891

[28] Lemon, P. W., Tarnopolsky, M. A., MacDougall, J. D., Atkinson, S. A.: Protein requirements and muscle mass/strength changes during intensive training in novice bodybuilders. J. Appl. Physiol. 73 (1992), 767-775

[29] Linn, T., Geyer, R., Prassek, S., Laube, H.: Effect of dietary protein intake on insulin secretion and glucose metabolism in insulin-dependent diabetes mellitus. J. Clin. Endocrinol. Metab. 81 (1996), 3938-3943

[30] Matthews, D. E., Campbell, R. G.: The effect of dietary protein intake on glutamine and glutamate nitrogen metabolism in humans. Am. J. Clin. Nutr. 55 (1992), 963-970

[31] Metges, C. C., Barth, C. A.: Metabolic consequences of a high dietary protein intake in adulthood: Assessment of the available evidence. J. Nutr. 130 (2000), 886-889

[32] Millward, D. J., Bowtell, J. L., Pacy, P., Rennie, M. J.: Physical activity, protein metabolism and protein requirements. Proc. Nutr. Soc. 53 (1994), 223-240

[33] Reeds, P. J., Hutchens, T. W.: Protein requirements: from nitrogen balance to functional impact. J. Nutr. 124 (1994), 1754S-1764S

[34] Remer, T., Pietrzik, K., Manz, F.: A moderate increase in daily protein intake causing an enhanced endogenous insulin secretion does not alter circulating levels or urinary excretion of dehydroepiandrosterone sulfate. Metabolism 45 (1996), 1483-1486

[35] Waterlow, J. C.: Protein requirements of infants: an operational assessment. Proc. Nutr. Soc. 49 (1990), 499-506

[36] Waterlow, J. C.: The requirements of adult man for indispensable amino acids. Eur. J. Clin. Nutr. 50 (Suppl 1) (1996), S151-S179

[37] WHO (World Health Organization): Energy and protein requirements. Report of the Joint FAO/WHO Expert Consultation, WHO Technical Report Series 724, Geneva (1985)

[38] Young, V. R., Borgonha, S.: Adult human amino acid requirements. Curr. Opin. Clin. Nutr. Metab. Care 2 (1999), 39-45

[39] Young, V. R., Zamora, J.: Effects of altering the proportions of essential to nonessential amino acids on growth and plasma amino acid levels in the rat. J. Nutr. 96 (1958), 21-27

[40] Zemel, M. B.: Calcium utilization: effect of varying level and source of dietary protein. Am. J. Clin. Nutr. 48 (Suppl) (1988), S880-S883

[41] Ziegler, E. E., Fomon, S. J.: Potential renal solute load of infant formulas. J. Nutr. 119 (Suppl 12) (1989), 1785-1788

Fat

A. Guiding values for intake

Age	Fat % of energy
Infants	
0 to under 4 months	45-50
4 to under 12 months	35-45
Children	
1 to under 4 years	30-40
4 to under 7 years	30-35
7 to under 10 years	30-35
10 to under 13 years	30-35
13 to under 15 years	30-35
Adolescents and adults	
15 to under 19 years	30[1]
19 to under 25 years	30[1]
25 to under 51 years	30[1,2]
51 to under 65 years	30
65 years and older	30
Pregnant women	
from the 4th month	30-35
Lactating women	30-35

[1] Very heavy manual labourers may need more

[2] Corresponds to 80 g of total fat for men with a guiding value for energy intake of 10 MJ (2400 kcal)

B. Explanations

Dietary fats are important energy sources, especially if the energy requirement is high (e.g. in heavy manual labourers). Their caloric value is more than twice that of carbohydrates and proteins.

Natural dietary fats consist nearly exclusively of a mixture of triglycerides; absorption in healthy individuals averages 98%. In patients with gastrointestinal

diseases, however, digestion and absorption may be influenced by the chain length of fatty acids, the number of their double bonds and the melting point of dietary fat.

Fatty acids are the most important component of dietary fat; they may be saturated, monounsaturated or polyunsaturated. The differences in chemical structure produce differences in physical (e.g. melting point) and biochemical behaviour (e.g. influence on plasma cholesterol concentration) (see below). The major part of saturated fatty acids in the body are of dietary origin; they may also be produced in the body by lipogenesis from glucose, however. Mono- and polyunsaturated fatty acids are also supplied with the diet or synthesized from saturated fatty acids. Polyunsaturated fatty acids with cis-configuration and certain positions of the double bonds are an exception. They are essential as they cannot be synthesized by the human organism (see page 45).

Dietary fat is also a source of fat-soluble vitamins and of flavour and aroma compounds. It is because of the latter that fat and dishes prepared with fat are much liked foods.

The general recommendation to reduce fat intake is based on epidemiological and clinical findings showing a close relation between high-fat diets - especially those containing saturated fat - and dyslipoproteinaemia and atherosclerosis [1, 2, 18, 19, 21, 22, 36] (see page 40) but also colon cancer [40] and overweight [25]. Too much fat in the diets of Germans, Austrians and Swiss, with fat providing > 35% to > 40% of dietary energy on a daily average and, consequently, diets supplying too much energy are one of the main reasons for the high incidence of overweight and elevated blood fat levels - both are risk factors for premature coronary heart disease [1, 23, 33, 34].

The results of epidemiological and intervention studies in humans suggest that fat intake providing 30% of dietary energy, with an adequate fatty acid pattern as part of a balanced mixed diet and in combination with sufficient physical activity may reduce the risk for myocardial infarction.

To achieve energy balance and an adequate intake of essential nutrients and other components of vegetable food which are beneficial to health (dietary fibre, phytochemicals) it is necessary to limit fat intake. Furthermore, reduced fat intake in a diet supplying low energy levels makes it easier to increase or at least maintain the necessary nutrient density.

Persons with light or moderate work should consume not more than 30% of energy in the form of fat. It is probably favourable even if only 25% are provided by fat because then more vegetable food will usually be consumed. In persons doing heavy muscle work and thus needing more energy, the share of fat in the

total energy supply may exceed the reference value by 5% in order to reduce the volume of food, and in persons doing extremely heavy work by up to 10%.

A fat intake by adults of up to 30% of total dietary energy, the proportion of long-chain saturated fatty acids should not exceed one third, i.e. 10% of total dietary energy. Polyunsaturated fatty acids should provide about 7% of dietary energy, and up to 10% if saturated fatty acids provide more than 10% of total energy, in order to prevent an increase in plasma cholesterol level [19]. Concurrently, intake of α-linolenic acid should be increased in order to lower the ratio of linoleic acid (n-6) to α-linolenic acid (n-3) to about 5 : 1 (see also pages 41 and 46). The rest is supplied by monounsaturated fatty acids, e.g. oleic acid, which may even account for more than 10% of total energy. If more than 30% of total energy are supplied from fat, surplus fat should primarily contain mono- and polyunsaturated fatty acids to prevent a rise in plasma cholesterol concentration (see pages 39 and 40). Simply put, at a total fat intake of 30% of dietary energy, saturated fatty acids (< 10% of energy) and unsaturated fatty acids (totalling 20% of energy and predominantly of plant origin) should be in a ratio of 1 : 2.

For their growth children and adolescents need additional energy especially during the first years of life and during puberty. The necessary high energy intake is facilitated by an increased proportion of dietary fat. Infants during the first months of life are dependent on a high dietary energy density which is only achieved by fat as the amount of food infants can ingest is limited. Already in children, however, close relations exist between diet, blood lipids and the development of changes in blood vessel walls. In the 2nd year of life, therefore, fat intake should be gradually reduced. Lowering fat intake to 30 - 35% of dietary energy seems to be practicable. Saturated fatty acids should account for not more than one third of dietary fat or 10% of dietary energy [10].

During pregnancy and lactation, fat intake may be increased to 35% of dietary energy. In old age fat should supply not more than 30% of dietary energy in order to adjust energy intake to the reduced energy needs. In physically very active older persons, the share of dietary fat may account for up to 35% of energy.

Dietary cholesterol

As food of animal origin often contains plenty of cholesterol besides saturated fatty acids, reduced intake of saturated fatty acids is also associated with a desirable reduction in cholesterol intake. Dietary cholesterol in fact raises the concentration of plasma cholesterol only to a small amount in terms of average values, but to a variable extent from person to person [11]. Also blood LDL cholesterol concentration is only increased to a small extent by dietary cholesterol compared to saturated fatty acids [19], but dietary cholesterol may intensify the

undesirable response of serum cholesterol to saturated fatty acids [11]. Dietary cholesterol intake, therefore, should not considerably exceed 300 mg/day [16].

Fatty acids, serum cholesterol and atherosclerosis

Plasma LDL and HDL cholesterol concentrations beyond the normal range are essential risk factors for cardiovascular diseases [1, 33]. They can be lastingly influenced by the dietary fat quantity, the proper ratio between saturated and unsaturated dietary fatty acids and by physical activity [16, 26, 41], but with great variability among individuals [11]. The saturated fatty acids lauric acid (C 12:0), myristic acid (C 14:0) and palmitic acid (C 16:0) increase plasma cholesterol concentration and especially the concentration of the unfavourable LDL cholesterol. Stearic acid (C 18:0) does not influence LDL cholesterol. Monounsaturated fatty acids, e.g. oleic acid (C 18:1 n-9), lower LDL cholesterol concentrations in cases where they replace dietary saturated fatty acids which would raise blood cholesterol. Polyunsaturated fatty acids, e.g. linoleic acid, actively lower the concentration of LDL cholesterol. However, also HDL cholesterol which has a favourable effect on the risk for atherosclerosis is somewhat lowered by linoleic acid, but less so by oleic acid [19].

Trans-fatty acids (see below) raise the concentration of LDL cholesterol in blood and lower the concentration of HDL cholesterol [12, 19]. The content of trans fatty acids in the human diet should, therefore, be as low as possible and their contribution to dietary energy kept below 1% [37] (see page 47, 48).

No evidence of the effects of conjugated linoleic acids (CLA) shown in animal experiments has yet been found in humans [12].

The plasma triglyceride level, another factor contributing to the risk of atherosclerosis, is raised by high intake of saturated fatty acids. Excessive energy intake generally leads to increased blood cholesterol and triglyceride concentrations.

The development of *atherosclerosis* is a multifactorial process. Besides individual disposition, plasma cholesterol may play a causal role in the setting of dyslipoproteinaemia. This also applies - frequently not only in an additive, but also in a synergistic sense - to other risk factors such as hypertension, diabetes mellitus, smoking, and even lack of physical activity. Relations among dietary fats, serum cholesterol and coronary heart disease discovered in epidemiological studies have been verified in experimental and clinical trials [15]. They have been further elucidated by studies on the effect of oxidized LDL [36]. Hence dyslipoproteinaemia may occasionally be the most important cause of early atherosclerosis; much more frequently, however, it is only one of several causes [35]. The complexity of the pathogenesis influences the results of intervention studies

which aim at preventing myocardial infarction by a change in diet. This goal could still be achieved in several of these studies using plasma cholesterol lowering diets [22, 26]. Experimental, controlled intervention studies combining a partly drastic reduction of fat intake (< 25% of energy) with a rigorous change in the patients' lifestyle have shown that there is even a chance of reversal of coronary heart disease [27, 31].

Dietary fatty acids influence not only the risk for atherosclerosis by changing the concentration and composition of blood lipoproteins. By changing the fatty acid pattern in blood-cell membranes, they also affect the rheological properties of blood. Via eicosanoids formed from n-6 and n-3 fatty acids, moreover, essential functions such as platelet aggregation, adhesion of monocytes to vessel walls, vascular dilatation, blood pressure and other parameters of the cardiovascular system are controlled. Added to these must be inflammatory processes and immune reactions [7, 24, 39]. Long-chain n-3 fatty acids are assumed to have an anti-arrhythmic effect as well [3, 5, 32].

Several intervention studies have shown protective effects of long-chain n-3 fatty acids, and of eicosapentaenoic acid (20:5 n-3) in particular, against fatal myocardial infarctions [4, 8, 14]. As an alternative to consumption of saltwater fish which is still not satisfactory, intake of α-linolenic acid (18:3 n-3) should rise. In the human organism, eicosapentaenoic acid [13, 38] is formed from α-linolenic acid as long as synthesis is not inhibited by high intake of linoleic acid (see page 46). From eicosapentaenoic acid, beneficial eicosanoids are formed [39]. In some of the observational studies, a significant inverse relation between intake of α-linolenic acid and the frequency of sudden cardiac death has been found [2, 9, 17, 28]. In patients after myocardial infarction, moreover, a significant decrease in the reinfarction rate by α-linolenic acid has been achieved in an intervention study [8] in which the ratio of linoleic acid (n-6) to α-linolenic acid (n-3) was about 4 : 1 [29]. In the sense of a preventive pattern of dietary polyunsaturated fatty acids in the diet of healthy individuals, DGE, ÖGE, SGE and SVE advocate a decrease in the ratio of linoleic acid (n-6) to α-linolenic acid (n-3) to 5 : 1 or lower.

Within the framework of Mediterranean diets, oleic acid is also assumed to protect against myocardial infarction and cancer. Little is known about the possible mechanisms, except for the effect on LDL and HDL cholesterol in blood, and specific long-term placebo-controlled intervention studies with oleic acid for prevention of myocardial infarction have yet to be carried out.

In adults, a prolonged total fat intake of more than 40% of dietary energy, and of more than 10% each of saturated and polyunsaturated fatty acids, is clearly unfavourable. More than 40% of dietary energy from fat promotes the development of atherosclerosis, colon cancer and obesity. Large amounts of saturated fatty acids increase the detrimental blood LDL cholesterol concentration.

Larger amounts of polyunsaturated fatty acids are also associated with a higher risk of lipid peroxide formation. In animal experiments, high intakes of polyunsaturated fatty acids promoted growth of tumours which had been induced by chemical carcinogens. However, there is no evidence of such a negative effect in humans [42]. n-3 Fatty acids are assumed to even protect against colon cancer.

However, high intake of long-chain n-3 fatty acids has been found to increase the disposition to haemorrhage and possibly to affect the functions of leucocytes and the immune system [6, 20, 30]. Intake of n-3 fatty acids should, therefore, not exceed 3% of dietary energy. For the total of polyunsaturated fatty acids, 10% of dietary energy are considered to be the upper limit.

To protect against oxidation of polyunsaturated fatty acids, the diet should also contain at least 0.4 mg of tocopherol equivalents per g of diene fatty acid equivalent (see pages 73 and 74)

References

[1] Abbott, R. D., Wilson, P. W., Kannel, W. B., Castelli, W. P.: High Density Lipoprotein Cholesterol, Total Cholesterol Screening, and Myocardial Infarction. The Framingham Study. Arteriosclerosis 8 (1988), 207-211

[2] Ascherio, A., Rimm, E. B., Giovannucci, E. L. et al: Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States. BMJ 313 (1996), 84-90

[3] Billmann, G. E., Hallaq, H., Leaf, A.: Prevention of ischemia-induced ventricular fibrillation by n-3 fatty acids. Proc. Natl. Acad. Sci. U.S.A. 91 (1994), 4427-4430

[4] Burr, M. L. et al.: Effects of changes in fat, fish and fiber intakes on death and myocardial reinfarction: diet and reinfarction trial. Lancet 2 (1989), 757-761

[5] Christensen, J. H., Gustenhoff, P., Korup, E. et al.: Effect of fish oil on heart rate variability in survivors of myocardial infarction: a double blind randomised controlled trial. BMJ 312 (1996), 677-678

[6] Clarke, J. T., Cullen-Dean, G., Regelink, E., Chan, L., Rose, V.: Increased incidence of epistaxis in adolescents with familial hypercholesterolemia treated with fish oil. J. Pediatr. 116 (1990), 139-141

[7] Connor, S. L., Connor, W. E.: Are fish oils beneficial in the prevention and treatment of coronary artery disease? Am. J. Clin. Nutr. 66 (1997), 1020S-1031S

[8] De Lorgeril, M., Salen, P., Martin, J.-L. et al: Mediterranean Diet, Traditional Risk Factors, and the Rate of Cardiovascular Complications After Myocardial Infarction. Final Report of the Lyon Diet Heart Study. Circulation 99 (1999), 779-785

[9] Dolecek, T. A.: Epidemiologic evidence of relationships between dietary polyunsaturated fatty acids and mortality in the Multiple Risk Factor Intervention Trial. Proc. Soc. Exp. Biol. Med. 200 (1992), 177-182

[10] ESPGAN Committee on Nutrition: Aggett, P., Haschke, F., Heine, W., Hernell, O., Koletzko, B., Lafeber, H., Ormisson, A., Rey, J., Tormo, R.: Committee report: childhood diet and prevention of coronary heart disease. J. Pediatr. Gastroenterol. Nutr. 19 (1994), 261-269

[11] Fielding, Chr. J., Havel, R. J., Todd, K. M. et al: Effects of Dietary Cholesterol and Fat Saturation on Plasma Lipoproteins in an Ethnically Diverse Population of Healthy Young Men. J. Clin. Invest. 95 (1995), 611-618

[12] Fritsche, J., Steinhart, H.: Analysis, occurrence, and physiological properties of trans fatty acids (TFA) with particular emphasis on conjugated linoleic acid isomers (CLA) - a review. Fett/Lipid 100 (1998), 190-210

[13] Gerster, H.: Can adults adequately convert α-linolenic acid (18:3n-3) to eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3)? Int. J. Vitam. Nutr. Res. 68 (1998), 159-173

[14] GISSI-Prevenzione Investigators: Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 354 (1999), 447-455

[15] Gotto, A. M., LaRosa, J. C., Hunninghake, D. et al: The cholesterol facts: A summary of the evidence relating dietary fats, serum cholesterol, and coronary heart disease. A joint statement by the American Heart Association and the National Heart, Lung, and Blood Institute. The Task Force on Cholesterol Issues, American Heart Association. Circulation 81 (1990), 1721-1733

[16] Hayes, K. C., Khosla, P.: Dietary fatty acid thresholds and cholesterolemia. FASEB J. 6 (1992), 2600-2607

[17] Hu, F. B., Stampfer, M. J., Manson, J. E., Rimm, E. B., Wolk, A., Colditz, G. A., Hennekens, Ch. H., Willett, W. C.: Dietary intake of α-linolenic acid and risk of fatal ischemic heart disease among women. Am. J. Clin. Nutr. 69 (1999), 890-897

[18] Hu, F. B., Stampfer, M. J., Manson, J. E. et al.: Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. Am. J. Clin. Nutr. 70 (1999), 1001-1008

[19] Katan, M. B., Zock, P. L., Mensink, R. P.: Effects of fats and fatty acids on blood lipids in humans: an overview. Am. J. Clin. Nutr. 60 (1994), 1017S-1022S

[20] Kelley, D. S., Branch, L. B., Love, J. E., Taylor, P. C., Rivera, Y. M., Jacono, J. M.: Dietary α-linolenic acid and immunocompetence in humans. Am. J. Clin. Nutr. 53 (1991), 40-46

[21] Kushi, L. H., Lew, R. A., Stare, F. J. et al: Diet and 20-year mortality from coronary heart disease. The Ireland-Boston Diet-Heart Study. N. Engl. J. Med. 312 (1985), 811-818

[22] Kwiterovich, P. O.: The effect of dietary fat, antioxidants, and pro-oxidants on blood lipids, lipoproteins, and atherosclerosis. J. Am. Diet. Assoc. 97 (1997) (Supplement), S31-S41

[23] Law, M. R., Wald, N. J., Thompson, S. G.: By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? BMJ 308 (1994), 367-373

[24] Nestel, P. J., Pomeroy, S. E., Sasahara, T. et al: Arterial compliance in obese subjects is improved with dietary plant n-3 fatty acid from flaxseed oil despite increased LDL oxidizability. Arterioscler. Thromb. Vasc. Biol. 17 (1997), 1163-1170

[25] Noack, R.: Nahrungsfett und Adipositas. Teil 1: Fett- und Kohlenhydrataufnahme und Nährstoffbilanzen. Ernährungs-Umschau 45 (1998), 8-13

[26] Oliver, M. F.: It is more important to increase the intake of unsaturated fats than to decrease the intake of saturated fats: evidence from clinical trials relating to ischemic heart disease. Am. J. Clin. Nutr. 66 (1997), 980S-987S

[27] Ornish, D., Scherwitz, L. W., Billings, J. H. et al: Intensive Lifestyle Changes for Reversal of Coronary Heart Disease. JAMA 280 (1998), 2001-2007

[28] Pietinen, P., Ascherio, A., Korhonen, P. et al: Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men: The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Am. J. Epidemiol. 145 (1997), 876-887

[29] Renaud, S., de Lorgeril, M., Delaye, J. et al: Cretan Mediterranean diet for prevention of coronary heart disease. Am. J. Clin. Nutr. 61 (suppl) (1995), S1360-S1367

[30] Saynor, R., Verel, D., Gillott, T.: The Long-Term Effect of Dietary Supplementation with Fish Lipid Concentrate on Serum Lipids, Bleeding Time, Platelets and Angina. Atherosclerosis 50 (1984), 3-10

[31] Schuler, G., Hambrecht, R., Schlierf, G., Niebauer, J., Hauer, K., Neumann, J., Hoberg, E., Drinkmann, A., Bacher, F., Grunze, M. et al.: Regular physical exercise and low-fat diet. Effects on progression of coronary artery disease. Circulation 86 (1992), 1-11

[32] Siscovick, D.S., Raghunathan, T.E., King, I., Weinmann, S. et al.: Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. JAMA 274 (1995), 1363-1367

[33] Stamler, J., Stamler, R., Neaton, J. D. et al.: Low Risk-Factor Profile and Long-term Cardiovascular and Noncardiovascular Mortality and Life Expectancy. Findings for 5 large cohorts of young adult and middle-aged men and women. JAMA 282 (1999), 2012-2018

[34] Stamler, J., Wentworth, D., Neaton, J. D.: Is relationship between serum cholesterol and risk of premature death from coronary heart disease continous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). JAMA 256 (1986), 2823-2828

[35] Steinberg, D.: The cholesterol controversy is over. Why did it take so long? Circulation 80 (1989), 1070-1078

[36] Steinberg, D., Parthasarathy, S., Carew, T. E. et al: Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. N. Engl. J. Med. 320 (1989), 915-924

[37] Steinhart, H., Fritsche, J.: Contents of trans fatty acids (TFA) in German foods and estimation of daily intake. Fett/Lipid 99 (1997), 314-318

[38] Valsta, L. M., Salminen, I., Aro, A., Mutanen, M.: α-Linolenic acid in rapeseed oil partly compensates for the effect of fish restriction on plasma long chain n-3 fatty acids. Eur. J. Clin. Nutr. 50 (1996), 229-235

[39] Wolfram, G.: Was sind und wie wirken ω-3-Fettsäuren? Ernährungs-Umschau 44 (1997), 36-41

[40] World Cancer Research Fund/American Institute for Cancer Research: Food, Nutrition, and the Prevention of Cancer: A Global Perspective (1997), 216

[41] Yu-Poth, S., Zhao, G., Etherton, T. et al: Effects of the National Cholesterol Education Program's Step I and Step II dietary intervention programs on cardiovascular disease risk factors: a meta-analysis. Am. J. Clin. Nutr. 69 (1999), 632-646

[42] Zock, P. L., Katan, M. B.: Linoleic acid intake and cancer risk: a review and meta-analysis. Am. J. Clin. Nutr. 68 (1998), 142-153

Essential fatty acids

A. Recommended intake

Age	Essential fatty acids	
	% of energy	
	n-6	n-3[1]
Infants		
0 to under 4 months	4.0	0.5
4 to under 12 months	3.5	0.5
Children		
1 to under 4 years	3.0	0.5
4 to under 7 years	2.5	0.5
7 to under 10 years	2.5	0.5
10 to under 13 years	2.5	0.5
13 to under 15 years	2.5	0.5
Adolescents and adults		
15 to under 19 years	2.5	0.5
19 to under 25 years	2.5	0.5
25 to under 51 years	2.5	0.5
51 to under 65 years	2.5	0.5
65 years and older	2.5	0.5
Pregnant women	2.5	0.5
Lactating women	2.5	0.5

[1] Estimated values

B. Explanations

Polyunsaturated fatty acids with cis-configuration and a certain position of double bonds are essential nutrients, as they cannot be synthesized in the human organism.

Besides n-6 fatty acids (linoleic acid = C 18:2 and the longer-chain fatty acids formed from linoleic acid, e.g. arachidonic acid = C 20:4), n-3 fatty acids are also needed (α-linolenic acid = C 18:3, and its longer-chain derivatives, especially

eicosapentaenoic acid = C 20:5 and docosahexaenoic acid = C 22:6). Both groups of fatty acids serve the purpose of forming functional structural lipids in tissues and regulatory eicosanoids. n-9 Fatty acids (e.g. oleic acid = C 18:1) and their longer-chain derivatives, in contrast, can be synthesized by humans.

Arachidonic acid, eicosapentaenoic acid and docosahexaenoic acid are essential parts of all cellular membranes. Eicosanoids formed from arachidonic acid (n-6) and eicosapentaenoic acid (n-3) influence the functions of smooth muscles, endothelium, monocytes and platelets as well as inflammatory and immune reactions, with partly antagonistic effects. Especially high concentrations of docosahexaenoic acid (n-3) are found in nervous tissue and in the photoreceptors of the retina.

In the biosynthesis of the physiologically important long-chain and highly unsaturated fatty acids, the fatty acids mentioned before compete with each other for the same enzyme system. Affinity decreases in the order of n-3, n-6, n-9 fatty acids. Because of this competition, the rate of conversion to the longer-chain derivatives depends, among other things, upon the dietary fatty acid pattern. Normally, at best 10% of the dietary essential fatty acids (linoleic acid and α-linolenic acid) are converted to the corresponding long-chain derivatives [5, 7].

The present reference values for intake of linoleic acid (n-6) and α-linolenic acid (n-3) are in the ratio of 5 : 1. Because the fatty acids compete with each other for the same enzyme system, an inadequate ratio of n-6 and n-3 fatty acids may affect the fatty acid pattern of growing tissue and the equilibrium of antagonistic eicosanoids [7, 14].

In cases of n-6 fatty acid deficiency (e.g. linoleic acid) the concentration of the so-called mead fatty acid (C 20:3 n-9) increases in serum and tissue, while in cases of n-3 fatty acid deficiency the content of docosapentaenoic acid (C 22:5 n-6) increases. n-6 Fatty acid deficiency may lead to eczema, fatty liver, anaemia, proneness to infections, wound healing disorders and retarded growth [4]. Symptoms of n-3 fatty acid deficiency (e.g. α-linolenic acid) are impaired vision, muscular weakness, trembling, and disorders of superficial and deep sensory function [2]. Essential fatty acid deficiency is very rare, however, as the fatty tissue of a normal weight adequately nourished adult contains more than 500 g of linoleic acid and 25 g of α-linolenic acid. A deficiency may be expected at most in patients with chronic fat malabsorption or on long-term fat-free artificial feeding [2, 3, 4].

A deficiency of very long-chain n-6 or n-3 fatty acids, especially arachidonic acid (n-6), eicosapentaenoic acid (n-3) or docosahexaenoic acid (n-3) may occur during the perinatal period (see below). It has never been diagnosed in healthy adults, however, because these fatty acids, although synthesized at a modest

rate, are in the long run produced in sufficient quantities.

In young healthy adults, the average requirement for linoleic acid has been found to be 6.5 g per day, or just under 2% of dietary energy [13]. Allowing for a coefficient of variation of 15%, the intake recommended for adults is about 2.5% of dietary energy. The estimate for n-3 fatty acids is 0.5% of the total dietary energy intake [2].

Measured against eicosanoid synthesis, linoleic acid and α-linolenic acid are biologically less potent than their longer-chain derivatives arachidonic and eicosapentaenoic acid. Activities should, therefore, be expressed in terms of (n-6) and (n-3) fatty acid equivalents. At present, in view of the lack of satisfactory data, such equivalents cannot be ultimately defined, however. Preliminary results of experiments lasting one or two weeks suggest that eicosapentaenoic acid, depending on the initial situation, is between 2 to > 10 times more potent than α-linolenic acid [1, 2, 3, 7, 12].

The fat of mature human milk contains on average 10 - 15% linoleic acid and > 1% α-linolenic acid, including their longer-chain derivatives. A fully breast-fed infant fed a daily volume of 750 ml breast milk with a mean fat content of 40 g/l receives about 3.0 - 4.5 g of linoleic acid daily [9]. For commercial infant formulae, ESPGAN calls for a linoleic acid level corresponding to 4.5 - 10.8% of energy content [6]. The ratio between linoleic acid and α-linolenic acid in commercial infant formulae should, as in human milk, be in the range of 5 : 1 to 15 : 1 [8]. As the long-chain polyunsaturated fatty acids docosahexaenoic acid (C 22:6 n-3) and arachidonic acid (C 20:4 n-6) may be conditionally essential nutrients due to the growth-related particularly high needs during early infancy, it is important that they are supplied with infant formulae [10].

In Germany, Austria and Switzerland, adequate intake of essential fatty acids, in terms of average values, is ensured. High levels of linoleic acid are contained in oils of vegetable sources such as sunflower oil, corn oil and soybean oil. Much α-linolenic acid is contained in linseed oil, walnut oil, rapeseed oil, and soybean oil. As the ratio of n-6 fatty acids to n-3 fatty acids should be less than 5 : 1, oils containing high levels of α-linolenic acid should be preferred. Oils with high levels of unsaturated fatty acids should contain at least 0.4 g of tocopherol equivalents per gram of diene fatty acid equivalent for protection against oxidation (see page 73, 74) Eicosapentaenoic acid and docosahexaenoic acid are contained mainly in fat saltwater fish such as herring, mackerel and salmon. They can contribute efficiently towards satisfying the requirement for essential n-3 fatty acids.

Cis-configuration is a prerequisite for the formation of eicosanoids and the biological efficacy of essential fatty acids. Unsaturated fatty acids with cis-configuration may be converted to fatty acids with trans-configuration by molecular

restructuring processes during partial hydrogenation of oils to margarines derived from vegetable sources. Trans fatty acids are also produced by bacteria in the rumen of cows; minor quantities are found in cow's milk fat. They increase the requirement for essential fatty acids, as they are competitive with them in the same enzyme systems. The content of trans fatty acids in the human diet should, therefore, be as low as possible; trans fatty acids should supply less than 1% of dietary energy [11].

Given gentle preparation methods and single use of frying fat, practically no losses of essential fatty acids occur.

A balanced mixed diet and diets for nutritional therapy of dyslipoproteinaemia and for reducing the risk for atherosclerosis provide children from 3 years as well as adolescents and adults with distinctly higher levels of polyunsaturated n-3 and n-6 fatty acids than those shown in the table for adequate essential fatty acid intake (see page 39).

References

[1] Adam, O., Wolfram, G., Zöllner, N.: Vergleich der Wirkung von Linolsäure und Eicosapentaensäure auf die Prostaglandinbiosynthese und Thrombozytenfunktion beim Menschen. Klin. Wochenschr. 64 (1986), 274-280

[2] Bjerve, K. S., Fischer, S., Wammer, F., Egeland, T.: α-Linolenic acid and long chain ω-3 fatty acid supplementation in three patients with ω-3 fatty acid deficiency: effect on lymphocyte function, plasma and red cell lipids, and prostanoid formation. Am. J. Clin. Nutr. 49 (1989), 290-300

[3] Bjerve, K. S., Mostad, I. L., Thoresen, L.: Alpha-linolenic acid deficiency in patients on long-term gastric-tube feeding: estimation of linolenic acid and long-chain unsaturated n-3 fatty acid requirement in man. Am. J. Clin. Nutr. 45 (1987), 66-77

[4] Collins, F. D., Sinclair, A. J., Royle, J. P. et al.: Plasma lipids in human linoleic acid deficiency. Nutr. Metab. 13 (1971), 150-167

[5] Demmelmair, H., Iser, B., Rauh-Pfeiffer, A., Koletzko, B.: Comparison of bolus versus fractionated oral applications of ^{13}C-linoleic acid in humans. Eur. J. Clin. Invest. 29 (1999), 603-609

[6] ESPGAN Committee on Nutrition: Aggett, P., Haschke, F., Heine, W., Hernell, O., Koletzko, B., Launiala, H. K., Rey, J., Rubino, A., Schöch, G., Senterre, J., Tormo, R.: Comment on the content and composition of lipids in infant formulas. Acta Paediatr. Scand. 80 (1991), 887-896

[7] Gerster, H.: Can adults adequately convert alpha-linolenic acid (18:3n-3) to eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3)? Int. J. Vitam. Nutr. Res. 68 (1998), 159-173

[8] Koletzko, B., Bremer, H. J.: Fat content and fatty acid composition of infant formulas. Acta Paediatr. Scand. 78 (1989), 513-521

[9] Koletzko, B., Thiel, I., Abiodun, P. O.: The fatty acid composition of human milk in Europe and Africa. J. Pediatr. 120 (1992), S62-70

[10] Koletzko, B.: Importance of dietary lipids. In: Tsang, R., Zlotkin, S. H., Nichols, B., Hansen, J. W. (eds.): Nutrition during infancy. Principles and practice. Digital Educational Publishing, Cincinnati (1997), 123-153

[11] Steinhart, H., Fritsche, J.: Contents of trans fatty acids (TFA) in German foods and estimation of daily intake. Fett/Lipid 99 (1997), 314-318

[12] Valsta, L. M., Salminen, I., Aro, A., Mutanen, M.: alpha-linolenic acid in rapeseed oil partly compensates for the effect of fish restriction on plasma long chain n-3 fatty acids. Eur. J. Clin. Nutr. 50 (1996), 229-235

[13] Wolfram, G., Zöllner, N.: Linolsäurebedarf des Menschen. In: Zöllner, N. (ed.): Wissenschaftliche Veröffentlichungen der Deutschen Gesellschaft für Ernährung 22, Steinkopff-Verlag, Darmstadt (1971), 51-60

[14] Wolfram, G.: Was sind und wie wirken ω-3-Fettsäuren? Ernährungs-Umschau 44 (1997), 36-41

Carbohydrates, dietary fibre

Guiding values for carbohydrate intake must consider individual energy requirements, the requirement for protein and the guiding values for fat intake. Fats and carbohydrates are the major sources of dietary energy. A balanced nutritious mixed diet should contain limited amounts of fat and plenty of carbohydrates (preferably starch) corresponding to more than 50% of total dietary energy [4, 5, 14].

A guiding value of > 50% of dietary energy from carbohydrates is substantiated by epidemiological findings showing that, otherwise, increased consumption of (saturated) dietary fats is directly related to the incidence of cardiovascular risk factors and other diseases [1, 10, 15, 19]. Altogether, a high intake of carbohydrates is advised as long as preference is given to food which contains plenty of starch, dietary fibre, essential nutrients and phytochemicals [16] (see page 196 and following pages). Isolated carbohydrates, especially mono- and disaccharides and refined or modified starches (e.g. maltodextrins) usually contain no essential nutrients; given adequate energy intake, they reduce nutrient density and essential nutrient supply [12, 13]. Very high intakes of these carbohydrates compromising nutrient density should therefore be avoided [5].

In Germany, Austria and Switzerland, according to the respective nutrition reports, the intake of carbohydrates providing about 40% of dietary energy is relatively low [3, 4, 6]. The trend of previous years and decades towards reduced intake of complex carbohydrates from cereal products and potatoes has turned, however, giving way to constant or moderately increasing consumption. Consumption of vegetables is trending up as well. Although intake of fresh fruit varies greatly, a certain increase has been recorded in Germany in recent years [4] while in Switzerland the trend is down [3].

According to the National Food Consumption Survey [4], the sex- and age-related intake of disaccharides (lactose included) is between 8.9% and 19%, that of monosaccharides between 4.7% and 8.4% of dietary energy [4]. The proportion of added sucrose (isolated cane/beet sugar) accounts for 6.3 - 13.2% of energy [12]. This means that more than half of dietary disaccharides originates from added sugar. For a preventive diet (see pages 38, 52 and 191) and in order to improve the basis for adequate intake of vitamins, minerals, trace elements, phytochemicals and dietary fibre, foods that reduce nutrient density should be even more replaced by fruit (fruit juice), vegetables (vegetable juice), salad and other carbohydrate sources such as whole-grain products and low-fat dairy products. Emphasis should be laid on polysaccharide-containing food while sugar intake should be moderate [5]. This applies particularly to low-energy diets (e.g. weight reduction diets or diets for elderly persons) and to children [13] and young adults [12].

Food components are more slowly absorbed from food naturally containing a large proportion of polysaccharides (starch) and dietary fibre. Food composition (i.e. whether carbohydrates are present alone or in combination with fat and protein) influences the absorption rate and thus utilization of carbohydrates in the organism.

From an energy point of view, the different energy supplying nutrients are equivalent. Under the influence of insulin but also at high intake, carbohydrates are the first to be oxidized or stored as glycogen. The preferential oxidation of carbohydrates is responsible for the fact that in diets with a too high energy content mainly dietary fatty acids are deposited in fatty tissue. It is only at very high carbohydrate intake (more than 400 - 500 g/day in young adults) that *de novo* synthesis of saturated fatty acids from glucose increases (to a lesser extent also from fructose); these saturated fatty acids are deposited in adipose tissue [15].

Adults metabolize at least 180 g glucose per day. Of this, about 140 g are combusted by the brain to carbon dioxide and water. The remaining 40 g of glucose are glycolytically degraded - mainly in erythrocytes - to lactate and pyruvate, from which glucose is synthesized again in the liver (Cori cycle). By physiological gluconeogenesis from amino acids, lactate or glycerol, about 130 g of glucose per day can be provided [14]. In this way the glucose requirement can largely be satisfied in the short term. In prolonged fasting, energy requirement of the brain, after adaptation of the metabolism, is met to a substantial extent by oxidation of ketone bodies. To avoid gluconeogenesis from protein and to inhibit lipolysis, at least 25% of dietary energy should be supplied from carbohydrates [5, 11].

In infants fed human milk during the 1st half year of life, about 45% of energy requirements are supplied from carbohydrates (48% from fat and 7% from protein). In human milk, the major part of carbohydrates is in the form of lactose, the rest are very complex oligosaccharides made up of a number of different monosaccharide components [9]. The physiological significance of these oligosaccharides is not exactly known. There is reason to assume that they influence the development of a specific intestinal flora and intestinal resistance to pathogenic bacteria and viruses.

In infant nutrition during the 2nd half year of life, carbohydrates provide about 47% of dietary energy (fat 40%, protein 13%) [7]. Beyond this age children fed a mixed diet obtain about 52% of their energy requirements from carbohydrates (35% from fat, 13% from protein).

The collective term **dietary fibre** comprises those components of vegetable food which are not degraded by physiological enzymes of the human gastrointestinal tract. Dietary fibre, except for lignin, stands for indigestible carbohydrates such as cellulose, hemicellulose, pectin, etc. Starch not digested by amylases

(resistant starch), and indigestible oligosaccharides such as oligofructose or oligosaccharides of the raffinose family (raffinose, stachyose, verbascose in pulses) should be included as well.

Dietary fibre fulfils several important and partly very different functions in the digestive tract and it influences metabolism [8, 17]. Dietary fibre is partly degraded in the colon by bacteria to short-chain fatty acids which lower the pH of the intestinal content and serve as nutrients for the intestinal mucosa. When they are absorbed, they provide additional energy of about 8.4 kJ (2 kcal) per gram of dietary fibre.

Dietary fibre is assumed to provide protection against several diseases, the most important of which are constipation, colon diverticulosis, colon cancer, gallstones, overweight, hypercholesterolaemia, diabetes mellitus, and atherosclerosis [2, 16, 17, 18]. When choosing fibre-rich foods one has to consider that individual fibre components differ in their effect. Dietary fibre should, therefore, be ingested from whole grains (mainly insoluble polysaccharides which are poorly degraded by bacteria) and from fruit, potatoes and vegetables (mainly soluble polysaccharides which are degraded by bacteria). This ensures a favourable distribution among insoluble and soluble dietary fibre.

For adults, the guiding value for intake of dietary fibre is at least 30 g per day, i.e. about 3 g/MJ (or 12.5 g/1000 kcal), in women, and 2.4 g/MJ (or 10 g/1000 kcal) in men. If energy intake is below the age- and sex-related guiding values, dietary fibre density must be higher than 3 g and 2.4 g/MJ, respectively (12.5 and 10 g/1000 kcal). For infants and children, no guiding values for dietary fibre intake can be set at present. Human milk contains oligosaccharides but no dietary fibre. When supplementary food *(Beikost)* is introduced, dietary fibre intake increases from about 1 g/MJ (or 4 g/1000 kcal), in the $5^{th}/6^{th}$ month to 2.4 g/MJ (or 10 g/1000 kcal) in the 12^{th} month [7]. Thus a guiding value for dietary fibre density of about 2.4 g/MJ (10 g/1000 kcal) seems to be practicable for children as well.

A potentially reduced absorption of polyvalent cations (calcium, magnesium, iron, zinc) is of practical importance only in cases of increased intake of isolated dietary fibre (e.g. bran for therapeutic reasons). A slightly reduced absorption rate associated with high fibre food is more than compensated for by its higher levels of polyvalent cations.

References

[1] Ascherio, A., Rimm, E. B., Giovannucci, E. L., Spiegelmann, D., Stampfer, M., Willet, W. C.: Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States. BMJ 313 (1996), 84-90

[2] Brown, L., Rosner, B., Willett, W. W., Sacks, F. M.: Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am. J. Clin. Nutr. 69 (1999), 30-42

[3] Bundesamt für Gesundheit (ed.): Vierter Schweizerischer Ernährungsbericht. Bern (1998)

[4] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/Main (1996)

[5] FAO/WHO: Carbohydrates in human nutrition. Report of a Joint FAO/WHO Consultation. FAO Food Nutr. Pap. 66, Rome (1998)

[6] Institut für Ernährungswissenschaften der Universität Wien (ed.); im Auftrag des Bundesministeriums für Frauenangelegenheiten und Verbraucherschutz und des Bundesministeriums für Arbeit, Soziales und Gesundheit: Österreichischer Ernährungsbericht 1998. Wien (1998)

[7] Kersting, M., Ness, B., Schöch, G.: Das Baukastensystem der Beikost zur Realisierung der Empfehlungen für die Nährstoffzufuhr im 5.-12. Lebensmonat. Akt. Ernähr.-Med. 19 (1994), 160-169

[8] Kritchevsky, D.: Dietary fiber. Annu. Rev. Nutr. 8 (1988), 301-328

[9] Kunz, C., Rudloff, S.: Biological functions of oligosaccharides in human milk. Acta Paediatr 82 (1993), 903-912

[10] Kushi, L. H., Lew, R. A., Stare, F. J., Ellison, C. R. et al: Diet and 20-year mortality from coronary heart disease. The Ireland-Boston Diet-Heart Study. N. Engl. J. Med. 312 (1985), 811-818

[11] Lifschitz, C. H.: Carbohydrate needs in preterm and term newborn infants. In: Nutrition during infancy. Tsang, R. C., Nichols, B. L. (eds.), Hanley & Belfus, Philadelphia (1988), 122-132

[12] Linseisen, J., Gedrich, K., Karg, G., Wolfram, G.: Sucrose intake in Germany. Z. Ernährungswiss. 37 (1998), 303-314

[13] Lyhne, N., Ovesen, L.: Added sugars and nutrient density in the diet of Danish children. Scand. J. Nutr. 43 (1999), 4-7

[14] MacDonald, I. L.: Carbohydrates. In: Modern Nutrition in Health and Disease. Shils, M. E., Olson, J. A., Shike, M. (eds.), 8th edition, Lea & Febiger, Philadelphia (1994), 36-46

[15] Noack, R.: Nahrungsfett und Adipositas. Teil 1: Fett- und Kohlenhydrataufnahme und Nährstoffbilanzen. Ernährungs-Umschau 45 (1998), 8-13

[16] Rimm, E. B., Ascherio, A., Giovannucci, E., Spiegelman, D., Stampfer, M. J., Willett, W. C.: Vegetable, Fruit, and Cereal Fiber Intake and Risk of Coronary Heart Disease Among Men. JAMA 275 (1996), 447-451

[17] Schneemann, B. O., Tietyen, J.: Dietary Fiber. In: Modern Nutrition in Health and Disease. Shils, M. E., Olson, J. A., Shike, M. (eds.). 8th edition, Lea & Febiger, Philadelphia (1994), 89-100

[18] Wolk, A., Manson, J. E., Stampfer, M. J. et al.: Long-term Intake of Dietary Fiber and Decreased Risk of Coronary Heart Disease Among Women. JAMA 281 (1999), 1998-2004

[19] World Health Organisation: Diet, Nutrition, and the Prevention of Chronic Diseases. Report of a WHO Study Group. WHO Technical Report Series 797, Geneva (1990)

Alcohol

Alcohol in beer, wine and distilled spirits has various effects. Important from the physiological point of view are the high energy density of alcohol, its adverse effect on intestinal absorption of many essential nutrients, and a potential displacement of vital dietary compounds in cases of alcohol abuse. In men aged 25 - 51 years about 7% of dietary energy is on average supplied from alcohol [4]. About 95% of ingested alcohol is used for generation of energy (29 kJ/g, or 7 kcal/g). About 5% is excreted in urine, sweat and expired air (here as acetaldehyde). Average alcohol and energy contents of the most common alcoholic beverages are listed in Table 1.

Table 1: Energy and alcohol content of alcoholic beverages [8]

Alcoholic berverage	Energy content MJ/l	Energy content kcal/l	Proportion of alcohol g/l	Proportion of alcohol in the caloric value (%)
Beer	1.6	390	35	63
Red wine, low alcohol	2.7	650	80	86
Red wine, high alcohol	3.2	775	95	86
White wine	2.9	700	85	85
Sparkling wine	3.5	835	90	75
Brandy	9.9	2400	330	96

Alcohol, if ingested on an empty stomach, lowers the blood sugar level, raises trigclyceride levels and blood pressure and shifts blood from the body's centre to its periphery, leading to reddening and a rise in skin temperature. Increased generation and release of heat raise the basal metabolic rate. The strong diuretic effect of alcohol may interfere with balance of some minerals. Nausea and vertigo after high alcohol consumption are due to an irritation of the gastric mucosa and to a direct influence on the vestibular system in the inner ear.

Even small doses of alcohol reduce muscular performance. Because of inhibition of activating and deactivating neurons, alcohol has both a sedative and stimulating effect on the central nervous system. With increasing blood alcohol level, these acute effects on the central nervous system lead to gait disturbances, prolonged reaction times and to inability to coordinate reactions. A blood alcohol concentration of more than 1.4 g/l is regarded as acute intoxication, which obscures consciousness to such extent that the drunkard is no longer accountable for his action.

In addition to these acute effects of alcohol, attention must also be paid to the long-term effects of chronic alcohol abuse, primarily the potential addiction which may ultimately produce severe consequences including damage to organs and the nervous system as well as confusion and psychic disorders.

Alcohol is to some extent metabolised in the gastric mucous membrane but primarily in the liver, in fact preferentially to other nutrients. Chronic alcohol consumption leads to fatty infiltration of the liver and later to liver cirrhosis. Added to this must be damage to other organs such as the pancreas and heart muscle [6]. Alcohol consumed in larger quantities and over prolonged periods, furthermore, increases the risk for cancer of the oral cavity, pharynx, oesophagus, breast and colon in humans of middle and older age [2, 5, 9]. Younger people are at greater risk for violent death especially in traffic accidents [1].

A cardioprotective effect of alcohol is due to a rise in blood HDL cholesterol, diminished platelet aggregation, decrease in fibrinogen and increased fibrinolysis [3, 7, 10]. However, advocacy of alcohol for prophylactic purposes is questionable as the negative effects of chronic alcohol consumption usually outweigh the positive ones.

A threshold value of alcohol intake beyond which the detrimental effects of alcohol outweigh potentially positive effects cannot be defined as the risks involved differ from individual to individual. Upon a cautious weighing of the effects of different alcohol quantities described in the literature, an intake of 20 g of alcohol per day in healthy men may be regarded as not injurious to health; however, this should not be consumed every day. Some epidemiological studies [2, 6] suggest that this dose may even be considered beneficial to health in relation to coronary risk in older men. For healthy women, only 10 g of alcohol per day can be regarded as compatible with health; this is because several epidemiological studies have shown the risk of damage to organs and breast cancer to increase at half the dose of alcohol for men [9]. Pregnant and lactating women are advised to completely abstain from alcohol to avoid any risk of alcohol related fetal pathology. 20 g of alcohol correspond to about 0.5 l of beer, 0.25 l of wine and 0.06 l of spirits.

References

[1] Andreasson, S., Allebeck, P., Romelsjö, A.: Alcohol and mortality among young men: logitudinal study of Swedish conscripts. BMJ 296 (1988), 1021-1025

[2] Boffetta, P., Garfinkel, L.: Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. Epidemiology 1 (1990), 342-348

[3] Criqui, M. H., Ringel, B. L.: Does diet or alcohol explain the French paradox? Lancet 344 (1994), 1719-1723

[4] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/Main (1996), 40

[5] Longnecker, M. P.: Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. Cancer Causes Control 5 (1994), 73-82

[6] Osswald, B. R., Seitz, H. K.: Alkoholabusus und seine Wirkungen. In: Echte und vermeintliche Risiken der Ernährung. Erbersdobler, H., Wolfram, G. (eds.), Wissenschaftliche Verlagsgesellschaft, Stuttgart (1993), 159-170

[7] Rimm, E. B., Klatsky, A., Grobbee, D., Stampfer, M. J.: Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine, or spirits? BMJ 312 (1996), 731-736

[8] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwerttabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[9] Thun, M. J., Peto, R., Lopez, A. D., Monaco, J. H., Henley, S. J., Heath, C. W. Jr., Doll, R.: Alcohol consumption and mortality among middle-aged and elderly U.S. adults. N. Engl. J. Med. 337 (1997), 1705-1714

[10] Wolfram, G.: Alkohol und Arteriosklerose. In: Alkoholische Getränke und Ernährungsmedizin. Kluthe, R., Kasper, H. (eds.), Georg Thieme Verlag, Stuttgart (1998), 47-52

Fat-soluble vitamins

Vitamin A (retinol), ß-carotene

A. Recommended intake

Age	Retinol			
	mg-equivalent[1]/day		mg-equivalent[1]/MJ[2] (Nutrient density)	
	m	f	m	f
Infants				
0 to under 4 months[3]		0.5	0.25	0.26
4 to under 12 months		0.6	0.20	0.21
Children				
1 to under 4 years		0.6	0.13	0.14
4 to under 7 years		0.7	0.11	0.12
7 to under 10 years		0.8	0.10	0.11
10 to under 13 years		0.9	0.10	0.11
13 to under 15 years	1.1	1.0	0.10	0.11
Adolescents and adults				
15 to under 19 years	1.1	0.9	0.10	0.11
19 to under 25 years	1.0	0.8	0.09	0.10
25 to under 51 years	1.0	0.8	0.10	0.10
51 to under 65 years	1.0	0.8	0.11	0.11
65 years and older	1.0	0.8	0.12	0.12
Pregnant women				
from the 4th month		1.1		0.12
Lactating women[4]		1.5		0.14

[1] 1 mg of retinol equivalent = 1 mg of retinol = 6 mg of all-trans-ß-carotene = 12 mg of other provitamin A carotenoids = 1.15 mg of all-trans-retinyl acetate = 1.83 mg of all-trans-retinyl palmitate; 1 IU = 0.3 µg of retinol

[2] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[3] Estimated value

[4] Allowance of about 70 µg of retinol equivalents per 100 g of secreted milk

B. Explanations

Vitamin A is of essential importance for growth, the immune system and the development of cells and tissue of quite different kinds. Retinoic acid, its active metabolite, regulates growth and constitution of skin and mucous membranes and thus, ultimately, also the functions of these. The aldehyde form of the vitamin, retinal, is important for the process of vision. Vitamin A alcohol, retinol, representing the homeostatically strictly controlled form of transport in the blood, is probably involved in spermatogenesis [1].

The early stage of vitamin deficiency escapes clinical-chemical diagnostics as the vitamin A concentration in the blood is still homeostatically regulated in the normal range even if the liver store is nearly completely depleted of vitamin A [7]. The first clinical sign of vitamin A deficiency is night blindness. It may appear simultaneously with or following the development of squamous metaplastic changes in the respiratory epithelium. The classical ocular signs of overt vitamin A deficiency are yellowish keratinized Bitot's spots on the conjunctival surface associated with xerophthalmia (drying of the lacrimal glands and conjunctiva). This may be followed by keratomalacia (corneal ulceration) with liquefaction of the corneal stroma, i.e. complete destruction of the arterior part of the eye, and irreversible blindness. In the presence of lowered resistance (compromised immune system due to vitamin A deficiency) infections normally taking a less severe course may be fatal. Vitamin A deficiencies of this kind are extremely rare in Western industrialized countries. In developing countries they are widespread and a major cause of blindness and increased mortality of children.

To assess an individual's vitamin A status, determination of serum retinol as the only parameter is not sufficient [7]. The relative dose response test (RDR test) is applied to check whether intake of 7.5 mg of retinol equivalents (RE) (25,000 IU of vitamin A) raises the vitamin serum concentration by more than 15%. If it does, a marginal vitamin A deficiency exists. In the case of a slight or no rise, vitamin status can be assumed to be adequate.

Groups with critical status are newborns, children with frequent infections as well as patients with measles, and elderly persons. The vitamin A status of the newborn greatly depends upon the supply during pregnancy. Infectious diseases with fever strongly increase vitamin A requirement [12, 13] with simultaneously elevated excretion [4, 17]. This should be primarily considered in small children whose vitamin A reserves are still low.

Growing insight into the mechanisms of vitamin A action has even added to the importance of an adequate intake. The absorption rate of retinol, which is a function of the amount and kind of dietary fat ingested, is not higher than 75%. Because of the great importance of the vitamin and of the few sources of

preformed dietary vitamin A (retinol), the human organism has built up liver stores of retinol esters; if adequately filled, they are capable of meeting the requirements, depending on age, for 1 - 3 weeks in newborn infants, 3 months in children and up to 1 year in adults [9, 10]. Hydrolysed to retinol, the vitamin is released from the store on two compounds, a retinol-binding protein formed in the liver and transthyretine (thyroxine-binding prealbumin) to which it is linked in the blood in the molar ratio of 1 : 1 : 1.

Besides the liver, other vitamin A-dependent tissues such as lungs, mucosa of the respiratory tract, eyes, various sensory epithelia, mucosa of the gastrointestinal tract, etc. also build up stores [2]. They obviously represent cellular reserves which can be used if the amount of retinol released from the blood to the cells is below the requirement. Depending on cellular vitamin expenditure, stores may be depleted within a more or less short time. It has not been established yet whether, and to what extent, such extrahepatic stores are replenished by retinol released from the liver or whether they are exclusively replenished via (postprandial) chylomicrons or LDL. Depleted stores of the target tissues impair the differentiation of epithelial cells leading to squamous metaplasia in the respiratory tract mucosa and thus to dysfunction of the tissue [18]. This explains why at the beginning stage of vitamin A deficiency, long before the classical ocular signs of deficiency appear, the susceptibility to respiratory infections is substantially increased [15].

Vitamin A requirement is satisfied by preformed vitamin A from food of animal origin (e.g. liver) and by provitamins (ß-carotene, some other carotenoids and ß-apo-carotenals) provided by plants. For a uniform assessment of requirement and adequate intake, the provitamins are calculated in terms of retinol equivalents (RE), a dietary concept which means a simplification for use in practice because combinations of food or methods of preparation may involve greater or lesser utilization of provitamins. Given a fully balanced and nutritious diet, however, the conversion factors indicated along with recommended intakes yield sufficiently accurate data about the provitamins' contribution to adequate vitamin A intake. International Units (IU) to express vitamin A activity are still used only in the pharmaceutical field.

Recommendations for adults are based on an experimentally determined average daily requirement of 0.6 mg of vitamin A (retinol). To allow for physiological variability, a coefficient of variation of not less than 30% has been considered adequate. Average requirement was therefore multiplied by 1.6 to arrive at the recommended intake. For women, an intake of 10 - 20% below that for men is recommended as the average plasma levels of women are lower (VERA study: women 1.78 µmol/l, men 2.04 µmol/l) [8].

During pregnancy more vitamin A is needed. Pregnant women should ingest on average one third more than women who are not pregnant. Because of the great

importance of the vitamin for the development and maturation of the lungs [1] a sufficient intake should be ensured especially in the 2nd and 3rd trimester of pregnancy. Liver (about 125 g/week) is the best source of vitamin A. Because liver, depending on the way animals were fed, may contain very high retinol levels, women in the 1st trimester of pregnancy should however abstain from eating liver (see below).

Infants ingest about 0.5 mg retinol equivalents per day along with the milk of healthy mothers [16]. With prolonged breast-feeding, the vitamin A content of human milk decreases while the breast-fed infant requires additional vitamin A for growth. Mainly for women breast-feeding longer than 4 months an allowance of 0.7 mg/day is recommended to satisfy their infant's requirement and to avoid deficits in the breast-feeding mother.

Reduced plasma vitamin A concentrations frequently observed at an advanced age are mostly the consequence of non-balanced diets.

Liver and vegetables with a high ß-carotene content (e.g. carrots, spinach or green cabbage) are particularly rich sources of vitamin A. Other foods of animal origin (fats, eggs, meat) contain relatively little vitamin A. In Europe in a mixed diet, about 25% of dietary vitamin A is supplied from provitamin A. If animal products, especially liver, are excluded from a diet, an adequate ß-carotene intake from vegetables must be ensured.

Losses of vitamin A occur under the influence of heat and light and in the presence of oxygen. Given diets customary in Central Europe and gentle food preparation, preparation losses for the total food prepared average about 20% [4]. Vitamin A activity of the provitamins is also reduced in the absence of oxygen by heat or light due to the formation of cis-isomers.

Given common dietary habits, adequacy of vitamin A intake can usually be assured.

Excessive doses of preformed vitamin A and of some retinoids (vitamin A derivatives such as retinoic acid which are used as medication) produce side-effects including acute symptoms such as headache and increased cerebral spinal fluid pressure; and chronic ones such as skin changes, jaundice, liver damage up to cirrhosis and painful skeletal changes (exostoses) [3]. Infants should receive doses of > 3 mg (> 10,000 IU) per day over a prolonged period only under medical control and for a clear indication, as such doses may lead to growth disturbance. In children disturbances of growth may also occur if they ingest more than 5 mg vitamin A per day over a prolonged time. Healthy adults should not ingest daily doses of more than 3 mg (10,000 IU) over longer periods (months - years) as, primarily in cases of predamaged liver, cirrhosis-like changes may appear which, however, are reversible after intake of the vitamin is stopped.

It has not been verified so far whether or not also high intakes of preformed vitamin A, of which partly high concentrations are contained in food (e.g. liver), may lead to fetal damage caused by formation of the solely teratogenic retinoic acid [3]. The latter is not present in food and food supplements. Women who are not sure they are pregnant or who plan to become pregnant should, therefore, not repeatedly ingest vitamin A doses of more than 3 mg retinol (corresponding to 10,000 IU) in addition to vitamin A intake from food in the early stages (1st trimester) of pregnancy. One portion (about 125 g) of liver usually contains 5 to 10 times, in extreme cases (depending on the way the animal was fed) even more than 20 times this dose. There is no danger that quantities exceeding safe vitamin A doses are supplied from other food or correctly dosed multivitamin preparations. Provitamins do not cause damage as absorption and conversion of provitamins to vitamin A are controlled - and limited - by the intestinal mucosa. The importance of adequate vitamin A intake during the 2nd and 3rd trimester of pregnancy has already been pointed out.

The upper limit of safe doses in adults is 3 mg (corresponding to 10,000 IU) of vitamin A per day.

ß-Carotene

ß-Carotene belongs to the group of carotenoids and fulfils two vital functions:
- ß-carotene (provitamin A) is a precursor of vitamin A and
- an antioxidative compound which, as like every other carotenoid, can protect against oxidative damage.

ß-Carotene can be ingested unchanged along with food and metabolized to vitamin A in different tissues (small intestine, liver, lungs). To answer the question of how much ß-carotene is needed by humans and whether this provitamin A is essential, two aspects have to considered:

- the efficiency and control of conversion to vitamin A, and
- the possibility of distinguishing an exclusive effect of ß-carotene from that of other carotenoids.

In the intestinal mucosa, about 17% of dietary ß-carotene and about 7% of a mixture of carotenoids are broken down to vitamin A. Cleavage of ß-carotene to vitamin A seems to increase with decreasing vitamin A intake, while with a satisfactory intake of vitamin A the cleavage rate decreases.

Bioavailability of ß-carotene varies greatly. This is possibly due to individual differences in fat absorption and less to the necessary presence of fat for ß-carotene absorption. There is no doubt that a certain amount of fat is

favourable to the absorption of fat-soluble vitamins; however, ß-carotene can also be absorbed in the absence of fat. Utilization of ß-carotene from vegetables largely depends on the kind of preparation - in carrots primarily on the mechanical destruction of plant cells (juice extraction, blanching). ß-Carotene is practically not absorbed from carrots ingested raw. High pectin levels in food may impair ß-carotene absorption.

ß-Carotene, in addition to other plant pigments, occurs in nearly every food of vegetable origin. Hence it is difficult to identify the non-provitamin A action of ß-carotene and its biological effect and essentiality for humans. The results of several epidemiological studies are furnishing increasing evidence that dietary carotenoids, independent of their provitamin A action, reduce the risk for cancer of the lungs, oesophagus and stomach [5, 6]. In theory, such effect could be very well explained: for carotenoids (the tomato pigment lycopene is even more potent than ß-carotene) are very active in degrading oxygen radicals and similar aggressive oxidants which have been known to promote, among other things, the formation of malignant neoplasms. They enter the organism in different ways, e.g. by environmental pollutants, but are also produced by the organism itself (e.g. to eliminate microorganisms).

As carotenoids accumulate in plasma and fatty tissue, their protective effect increases with increasing quantity ingested. ß-Carotene, strictly speaking, is a marker or indicator of the amount of vegetables and certain fruit ingested. Good sources are dark green vegetables (e.g. spinach, green cabbage, green beans, broccoli, lamb's lettuce). Carrots are indeed rich in carotene but it is only available when carrots are prepared as described above.

So far, there has been uncertainty about the required daily intake of ß-carotene (see also section II, pages 194 and 195). Some orientation is provided by studies using either calculated ß-carotene intakes or ß-carotene blood concentrations resulting from dietary intake as indicators of the prophylactic effects of ß-carotene and the carotenoids. From such studies an estimated range of 2 - 4 mg per day may be derived.

In large epidemiological studies lasting several years a daily intake of up to 10 mg of dietary ß-carotene has been shown to be harmless. However, results obtained from two intervention studies with ß-carotene [11, 19] are reason to question the harmlessness of higher ß-carotene doses (20 and 30 mg) in heavy smokers. Further research is necessary to evaluate higher doses, in compound and single preparations, over a longer period in different age groups.

References

[1] Biesalski, H. K.: Vitamin A und Retinoide. In: Biesalski, H. K., Schrezenmeir, J., Weber, K., Weiß, H. (eds.). Vitamine. Physiologie, Pathophysiologie, Therapie. Thieme Verlag, Stuttgart (1997), 3-33

[2] Biesalski, H. K., Weiser, H.: Microdetermination of Retinyl Esters in Guinea Pig Tissues under Different Vitamin-A-Status Conditions. J. Micronutr. Analysis 7 (1990), 97-116

[3] Biesalski, H. K.: Comparative Assessment of the Toxicology of Vitamin A and Retinoic Acid. Toxicology 57 (1989), 117-161

[4] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[5] Flagg, E. W., Coates, R. J., Greenberg, R. S.: Epidemiologic studies of antioxidants and cancer in humans. J. Am. Coll. Nutr. 14 (1995), 419-427

[6] Garewal, H.: Antioxidants in oral cancer prevention. Am. J. Clin. Nutr. 62 (1995), 1410S-1416S

[7] Gerlach, T., Biesalski, H. K., Bässler, K. H.: Serum-Vitamin-A-Bestimmungen und ihre Aussagekraft zum Vitamin-A-Status. Z. Ernährungswiss. 27 (1988), 57-70

[8] Heseker, H., Schneider, R., Moch, K.J., Kohlmeier, M., Kübler, W.: Vitaminversorgung Erwachsener in der Bundesrepublik Deutschland. In: Kübler, W., Anders, H.J., Heeschen, W., Kohlmeier, M. (eds.): VERA-Schriftenreihe Bd. IV, Wiss. Fachverlag Dr. Fleck, Niederkleen (1992)

[9] Olson, J. A.: Evaluation of vitamin A status in children. World Rev. Nutr. Diet 31 (1978), 130-134

[10] Olson, J. A.: Serum levels of vitamin A and carotenoids as reflectors of nutritional status. J. Natl. Cancer Inst. 73 (1984), 1439-1444

[11] Omenn, G. S., Goodman, G. E., Thornquist, M. D., Balmes, J., Cullen, M. R., Glass, A., Keogh, J. P., Meyskens, F. L., Valanis, B., Williams, J. H., Barnhart, S., Hammar, S.: Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. N. Engl. J. Med. 334 (1996), 1150-1155

[12] Rahman, M. M., Mahalanabis, D., Alvarez, J. O. et al: Acute respiratory infections prevent improvement of vitamin A status in young infants supplemented with vitamin A. J. Nutr. 126 (1996), 628-633

[13] Rosales, F. J., Ritter, S. J., Zolfaghari, R. et al: Effects of acute inflammation on plasma retinol, retinol-binding protein, and its mRNA in the liver and kidneys of vitamin A-sufficient rats. J. Lipid Res. 37 (1996), 962-971

[14] Semba, R. D.: Vitamin A, immunity, and infection. Clin. Infect. Dis. 19 (1994), 489-499

[15] Sommer, A., Katz, J., Tarwotjo, I.: Increased risk of respiratory disease and diarrhea in children with preexisting mild vitamin A deficiency. Am. J. Clin. Nutr. 40 (1984), 1090-1095

[16] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[17] Stephensen, C. B., Alvarez, J. O., Kohatsu, J. et al: Vitamin A is excreted in the urine during acute infection. Am. J. Clin. Nutr. 60 (1994), 388-392

[18] Stofft, E., Biesalski, H. K., Zschaebitz A., Weiser, H.: Morphological Changes in the Tracheal Epithelium of Guinea Pigs in Conditions of "Marginal" Vitamin A Deficiency. A light, scanning- and transmission-electron microscopic study under special breeding conditions appropriate to early vitamin A deficiency. Int. J. Vitam. Nutr. Res. 62 (1992), 134-142

[19] The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group: The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N. Engl. J. Med. 330 (1994), 1029-1035

Vitamin D (calciferols)

A. Recommended intake

Age	Vitamin D[1]		
	µg/day	µg/MJ[2] (Nutrient density)	
		m	f
Infants[3]			
0 to under 4 months	10	5.0	5.3
4 to under 12 months	10	3.3	3.4
Children			
1 to under 4 years	5	1.1	1.1
4 to under 7 years	5	0.8	0.9
7 to under 10 years	5	0.6	0.7
10 to under 13 years	5	0.5	0.6
13 to under 15 years	5	0.4	0.5
Adolescents and adults			
15 to under 19 years	5	0.5	0.6
19 to under 25 years	5	0.5	0.6
25 to under 51 years	5	0.5	0.6
51 to under 65 years	5	0.5	0.7
65 years and older	10	1.2	1.4
Pregnant women	5		0.5
Lactating women	5		0.5

[1] 1 µg = 40 IU; 1 IU = 0.025 µg

[2] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[3] The German Paediatric Society (*Deutsche Gesellschaft für Kinderheilkunde*) recommends for prophylaxis of rickets in breast-fed and non breast-fed infants a vitamin D tablet of 10 – 12.5 µg (400 – 500 IU) daily, starting upon completion of the 1st week of life up to the end of the 1st year of life, independently of vitamin D production by UV light in the skin and vitamin D intake from human milk or infant formulae (basic vitamination). Prophylaxis may be continued in the winter months of the 2nd year of life.

B. Explanations

The vitamin D group comprises several biologically active compounds called calciferols. One distinguishes between vegetable ergocalciferol (Vitamin D_2) and cholecalciferol (vitamin D_3) present in food of animal origin. Humans are capable of synthesizing vitamin D_3 from its precursor dehydrocholesterol in the skin in a process involving ultraviolet light of the wavelength 290 - 315 nm (UVB light). Cholecalciferol formed endogenously in the skin or ingested with food of animal origin can be defined as pre-prohormone which, by hydroxylation at Carbon-atom 25, is converted in the liver to the prohormone 25-hydroxy-cholecalciferol (25-hydroxyvitamin D). This metabolite (calcidiol) is again hydroxylated (at Carbon-atom 1) in the kidneys giving rise to the vitamin D hormone 1,25-dihydroxycholecalciferol (= calcitriol). Ergocalciferol of plant origin which may be present in food in small quantities is metabolized in the same way. Vitamin D_2 and vitamin D_3 are about equally potent in humans. The final metabolism includes another hydroxylation and degradation step. The most important end product excreted in urine probably is calcitrinic acid. About 40 metabolites are known altogether.

Vitamin D hormones are needed for regulation of calcium homeostasis and phosphate metabolism. On a molar basis, the vitamin D hormone calcitriol is the most potent activator of intestinal calcium absorption [2]. Calcitriol, furthermore, increases intestinal phosphate absorption and tubular calcium reabsorption and is involved in bone mineralization. Calcitriol influences the differentiation of epithelial cells of the skin and modulates cellular activity in the immune system [11]. It binds to about 30 target organs with nucleoreceptors and influences the transcription of hormone sensitive genes, thus controlling synthesis of several proteins. Also calcidiol increases calcium absorption [22]. For an optimal vitamin D effect adequate calcium intake is necessary, and vice versa (see page 141).

Vitamin D deficiency interferes with calcium homeostasis and phosphate metabolism. In infants and small children, hypovitaminosis D leads to rickets which, due to insufficiently mineralized (or calcified) bone matrix, is accompanied by skeletal deformations and enlargement of the epiphyses of joints (rachitic beads, bowlegs, craniomalacia, quadrate skull). Other symptoms are reduced muscular strength, lowered muscle tone and increased susceptibility to infection.

In adults, *overt* vitamin D deficiency leads to osteomalacia which is characterized by demineralization and restructuring processes of fully developed bones. Typical are band-shaped restructuring zones (Looser's), in which spontaneous fractures may occur, and slow bending or bowing of long bones. Affected persons suffer from generalized pains involving the whole skeleton, and myopathy. Suboptimal vitamin D supply is one of the causes of osteoporosis at advanced age. Different from osteomalacia, osteoporosis is characterized by reduction of

inorganic and organic bone tissue and simultaneous coarsening of its structure. A high incidence of hip fractures has been regarded as a consequence of an inadequate vitamin D supply [17].

Vitamin D status is determined best by the plasma level of 25-hydroxyvitamin D. Normal blood levels of this metabolite and normal blood concentrations of calcium, phosphorus, alkaline phosphatase and parathyroid hormone suggest adequate supply. Overt vitamin D deficiency with increased risk for rickets and osteomalacia is diagnosed in the presence of serum 25-hydroxyvitamin D levels of < 10 nmol/l (< 4 ng/ml). Elevated parathyroid hormone levels (secondary hyperparathyroidism) are already found at serum concentrations of 25-hydroxyvitamin D between 10 and 25 nmol/l (4 - 10 ng/ml; suboptimal range). If calcium intake is insufficient, increased parathyroid hormone concentrations may already occur at 25-hydroxyvitamin D levels of 20 - 50 nmol/l (10 - 20 ng/ml).

Recommendations are made in weight units of the vitamins D_2 and D_3 (1 µg of ergocalciferol or cholecalciferol = 40 IU). The quantities recommended only refer to vitamin D ingested orally. If there is adequate exposure to UVB, dietary intake of vitamin D is not required. Dietary vitamin D requirement thus depends on several external factors of geographic, climatic and cultural nature which influence vitamin D synthesis in the skin. They include latitude, season, time of day, weather and clothing. Other influencing factors are skin pigmentation and age [7, 13].

In infants, regular exogenous vitamin D intake is of great importance. As human milk is insufficient to cover the requirement, vitamin D supplements should be given regularly for prophylactic purposes. A daily vitamin D intake of 2.5 µg or 5 µg protects infants against rickets [19]. This does not ensure 25-hydroxyvitamin D levels above 25 nmol/l (10 ng/ml) in all infants, however. Taking the climatic conditions of Central Europe into account and including a safety allowance, a daily dose of 10 - 12.5 µg of vitamin D (400 - 500 IU) is recommended for the whole period of infancy independent of the season.

Vitamin D intake recommended for infants fed commercial infant formulae has been based on the requirement of breast-fed infants. The fortification of infant food, especially commercial infant formulae, with vitamin D should be regarded as basic vitamin provision (silent prophylaxis of rickets). Infants fed such formulae should still receive additional doses of vitamin D. No disadvantage will result from a daily total vitamin intake from commercial infant formulae and a vitamin D supplement at the recommended dose of up to 20 µg = 800 IU; higher doses should only be applied in special cases and upon medical advice (because of reduced absorption and increased requirement, pre-term infants receive daily doses of up to 25 µg of vitamin D during the first two to three months of life).

In small children who were adequately supplied with vitamin D during infant age,

rickets is rare. Exposure to the open air and UV light ensure efficient synthesis of vitamin D in the skin. Extra care is needed for the prophylaxis in dark pigmented people, and especially their children, living in northern regions.

Maximal bone mass is reached as late as in the 3rd decade of life. Vitamin D supply necessary for optimal development of bone mass is not exactly known and difficult to estimate in view of the fact that endogenous synthesis satisfies requirement provided UV exposure is sufficient. Daily intake of 5 µg vitamin D is recommended over the whole period of growth. In Germany beyond infant age the vitamin D intake (25th to 75th percentile) from an otherwise adequate diet is between 2.1 and 6.9 µg of vitamin D per day, depending on age and sex [1].

Via the placenta and with breast milk, fetuses and infants, respectively, receive relatively small quantities of vitamin D. During pregnancy, an increase in calcitriol production is the reason for a relatively small additional requirement. Increasing vitamin D intake during pregnancy and lactation beyond the recommended age-related amounts is not necessary.

In old age, the capability of synthesizing vitamin D in the skin is much lower than in young adults [13]. Less time spent outdoors meaning less exposure to UV light further reduces endogenous production of vitamin D, e.g. in homebound elderly persons. There is sufficient evidence that symptoms of vitamin D deficiency are wide-spread among the elderly [6, 15, 18, 20]. Increased vitamin D intake may correct secondary hyperparathyroidism [14], retard bone degradation processes [3], and, in combination with adequate calcium intake, lower the risk of bone fractures [4]. Possibly for optimal vitamin D effects in the elderly (above 70 years) an intake of 15 - 20 µg per day may be needed. Not enough data are available at present, however, to justify a general recommendation of > 10 µg per day.

Vitamin D is absorbed with dietary fat and transported from the intestine in chylomicrons via the lymphatic system. About 80% has been found to be absorbed. Vitamin D status is impaired by disorders of fat digestion and absorption, e.g. in lack of bile acids, coeliac disease or exocrine pancreatic insufficiency. In severe hepatic diseases and renal insufficiency conversion of cholecalciferol to the active metabolites may be affected. Long term use of antiepileptics and hypnotics (e.g. barbiturates) increases vitamin D requirement up to 25 µg per day due to accelerated metabolism; without supplementation, hypovitaminosis D (antiepileptic osteopathy) follows in up to 10% of cases [16].

Only few foods, among them especially cod-liver oil, fatty fish (e.g. herring and mackerel), liver, margarine (vitamin D-fortified) and egg yolk contain vitamin D in appreciable quantities. Storage and preparation of food do not substantially influence vitamin D activity. Given the usual cooking times, it is resistant to heat of up to 180° C; in food, it is only susceptible to oxygen and light. Preparation losses average 10%.

In persons with intact metabolism, vitamin D intoxication can only result from excessive oral intake, not from excessive exposure of the skin to UV light. Usually calcitriol levels are not, or only slightly elevated while 25-hydroxyvitamin D levels in the plasma increase massively [10]. Increased intestinal calcium absorption and elevated calcium mobilization from bones raise plasma calcium concentration which, as hypercalcaemia syndrome, may lead to severe organ disorders: frequent urination and thirst, nausea and vomiting, depressive illness, renal stones, nephrocalcinosis and renal insufficiency [5]. Fatal vitamin D intoxications have been reported [21]. In infants, daily doses of more than 25 µg may only be administered following a strict indication; regular controls of plasma calcium concentrations and urinary calcium excretion are advised. The earlier practice of intermittent high-dose vitamin D prophylaxis of rickets is now outdated. For adults, a daily vitamin D intake up to 50 µg is not considered injurious to health [8, 9]. After prolonged intake of 95 µg/day cases of hypercalcaemia (> 11 mg/dl = 2.75 mmol/l) were observed [12].

References

[1] Adolf, T., Schneider, R., Eberhardt, W., Hartmann, S., Herwig, A., Heseker, H., Hünchen, K., Kübler, W., Matiaske, B., Moch, K. J., Rosenbauer, J.: Ergebnisse der Nationalen Verzehrsstudie (1985-1988) über die Lebensmittel- und Nährstoffaufnahme in der Bundesrepublik Deutschland. In: VERA-Schriftenreihe Band XI. W. Kübler, H. J. Anders, W. Heeschen (eds.), Wissenschaftlicher Fachverlag Dr. Fleck, Niederkleen (1995)

[2] Barger-Lux, M. J., Heaney, R. P., Lanspa, S. J., Healy, J. C., DeLuca, H. F.: An investigation of sources of variation in calcium absorption efficiency. J. Clin. Endocrinol. Metab. 80 (1995), 406-411

[3] Brazier, M., Kamel, S., Maamer, M., Agbomson, F., Elesper, I., Garabedian, M., Desmet, G., Sebert, J. L.: Markers of bone remodeling in the elderly subject: effects of vitamin D insufficiency and its correction. J. Bone Miner. Res. 10 (1995), 1753-1761

[4] Chapuy, M. C., Arlot, M. E., Duboeuf, F., Brun, J., Crouzet, B., Arnaud, S., Delmas, P. D., Meunier, P. J.: Vitamin D_3 and calcium to prevent hip fractures in the elderly women. N. Engl. J. Med. 327 (1992), 1637-1642

[5] Chesney, R. W.: Vitamin D: can an upper limit be defined? J. Nutr. 119 (1989), 1825-1828

[6] Gloth, F. M. 3rd., Gundberg, C. M., Hollis, B. W., Haddad, J. G. Jr., Tobin, J. D.: Vitamin D deficiency in homebound elderly persons. JAMA 274 (1995), 1683-1686

[7] Holick, M. F.: McCollum Award Lecture, 1994: Vitamin D - New Horizons for the 21st century. Am. J. Clin. Nutr. 60 (1994), 619-630

[8] Honkanen, R., Alhava, E., Parviainen, M., Talasniemi, S., Monkkonen, R.: The necessity and safety of calcium and vitamin D in the elderly. J. Am. Geriatr. Soc. 38 (1990), 862-866

[9] Johnson, K. R., Jobber, J., Stonawski, B. J.: Prophylactic vitamin D in the elderly. Age Ageing 9 (1980), 121-127

[10] Markestad, T., Hesse, V., Siebenhuner, M., Jahreis, G., Aksnes, L., Plenert, W., Aarskog, D.: Intermittent high-dose vitamin D prophylaxis during infancy: effect on vitamin D metabolites, calcium, and phosphorus. Am. J. Clin. Nutr. 46 (1987), 652-658

[11] Merke, J., Ritz, E., Schettler, G.: Neue Gesichtspunkte zur Rolle von Vitamin D. Dtsch. Med. Wschr. 111 (1986), 345-349

[12] Narang, N. K., Gupta, R. C., Jain, M. K.: Role of vitamin D in pulmonary tuberculosis. J. Assoc. Physicians India 32 (1984), 185-188

[13] Need, A. G., Morris, H. A., Horowitz, M., Nordin, C.: Effects of skin thickness, age, body fat, and sunlight on serum 25-hydroxyvitamin D. Am. J. Clin. Nutr. 58 (1993), 882-885

[14] Offermann, G., Biehle, G.: Vitamin D-Mangel und Osteomalazie beim alten Menschen. Dtsch. Med. Wochenschr. 103 (1978), 415-419

[15] Offermann, G., Pinto, V., Kruse, R.: Antiepileptic drugs and vitamin D supplementation. Epilepsia 20 (1979), 3-15

[16] Ooms, M. E., Roos, J. C., Bezemer, P. D., van der Vijgh, W. J., Bouter, L. M., Lips, P.: Prevention of bone loss by vitamin D supplementation in elderly women: a randomized double-blind trial. J. Clin. Endocrinol. Metab. 80 (1995), 1052-1058

[17] Peacock, M.: Nutritional aspects of hip fractures. In: Nutritional Aspects of Osteoporosis '94. P. Burckhardt, R. P. Heaney (eds.), Ares Serona Symposia, Publications, Rome, Italy (1995), 213-222

[18] Scharla, S. H., Scheidt-Nave, C., Leidig, G., Woitge, H., Wüster, C., Seibel, M. J., Ziegler, R.: Lower serum 25-hydroxyvitamin D is associated with increased bone resorption markers and lower bone density at the proximal femur in normal females: a population-based study. Exp. Clin. Endocrinol. Diabetes 104 (1996), 289-292

[19] Specker, B. L., Ho, M. L., Oestreich, A., Yin, T. A., Shui, Q. M., Chen, X. C., Tsang, R. C.: Prospective study of vitamin D supplementation and rickets in China. J. Pediatr. 120 (1992), 733-739

[20] Schmidt-Gayk, K., Wahl, R., Jung, H. H., Goossen, J., Röher, H. D.: Vitamin D-Mangel bei Schenkelhalsfrakturen. Münch. Med. Wochenschr. 120 (1978), 1167-1171

[21] Wolf, H.: Alternative Rachitisprophylaxe mit optischer Strahlung. Pädiatr. Prax. 28 (1983), 629-638

[22] Zittermann, A., Scheld, K., Stehle, P.: Seasonal variations in vitamin D status and calcium absorption do not influence bone turnover in young women. Eur. J. Clin. Nutr. 52 (1998), 501-506

Vitamin E (tocopherols)

A. Estimated values for adequate intake

Age	Tocopherol mg-equivalent[1,2]/day	
	m	f
Infants		
0 to under 4 months	3	3
4 to under 12 months	4	4
Children		
1 to under 4 years	6	5
4 to under 7 years	8	8
7 to under 10 years	10	9
10 to under 13 years	13	11
13 to under 15 years	14	12
Adolescents and adults		
15 to under 19 years	15	12
19 to under 25 years	15	12
25 to under 51 years	14	12
51 to under 65 years	13	12
65 years and older	12	11
Pregnant women		13
Lactating women[3]		17

[1] 1 mg of RRR-α-tocopherol equivalent = 1 mg of RRR-α-tocopherol = 1.49 IU; 1 IU = 0.67 mg of RRR-α-tocopherol = 1 mg of all-rac-α-tocopheryl acetate

[2] 1 mg of RRR-α-tocopherol (D-α-tocopherol) equivalent = 1.1 mg of RRR-α-tocopheryl acetate (D-α-tocopheryl acetate) = 2 mg of RRR-β-tocopherol (D-β-tocopherol) = 4 mg of RRR-γ-tocopherol (D-γ-tocopherol) = 100 mg of RRR-δ-tocopherol (D-δ-tocopherol) = 3.3 mg of RRR-α-tocotrienol (D-α-tocotrienol) = 1.49 mg of all-rac-α-tocopheryl acetate (D,L-α-tocopheryl acetate)

[3] Allowance of about 260 µg of RRR-α-tocopherol equivalents per 100 g of secreted milk

B. Explanations

Vitamin E is the nutritional term for a group of chemical compounds which all contain a molecular ring system (chroman ring) with a free or esterified OH group and a saturated or unsaturated isoprenoidal side chain (16 Carbon atoms).

One differentiates among α-, β-, γ- and δ-tocopherol, depending on the number and distribution of methyl (CH_3) groups at the chroman ring. According to current nomenclature, natural tocopherols have the RRR-configuration, e.g. RRR-α-tocopherol (formerly D-tocopherol). Corresponding molecules with an unsaturated side chain are called tocotrienols.

Naturally occurring tocopherols are exclusively synthesized by plants. There, and in the animal organism as well, they act as a protective system against reactive oxygen (free radical, singlet oxygen) and thus prevent mainly polyunsaturated fatty acids in the membrane lipids from being peroxidized. In fact, tocopherol *in vivo* acts as one of the most potent protective systems against lipid peroxidation. It inhibits formation of oxidized LDL, in plasma which are a major risk factor for atherosclerosis. It is supported in this function by non-enzymatic (e.g. vitamin C, ß-carotene) and enzymatic (e.g. selenium containing glutathione peroxidases) systems. In this context vitamin E influences eicosanoid synthesis and the immune system, the cholesterol-phospholipid ratio in membranes (membrane fluidity) and is indirectly involved in cellular respiration [2].

Vitamin E deficiency in humans leads to several disturbances of membrane function, muscle metabolism and the nervous system due to an accumulation of radicals and lipid peroxidation [12].

These reactions must be expected to appear when vitamin E is not absorbed or utilized. It is only in extreme cases, however, that vitamin E deficiency can be derived from biochemical parameters. In cases of A-ß-lipoproteinaemia it takes years for neuropathy involving the central and peripheral nervous system, retina and skeletal muscles to occur. Vitamin E deficiency may also follow intestinal resection and appear in severe hepatic diseases (e.g. biliary cirrhosis) and (less frequently) mucoviscidosis. In prematurely born infants, haemolytic anaemia had occasionally been diagnosed before tocopherol supplemented formulae became available.

The protective capacity of individual tocopherols in different animal species has been taken as a measure of their potency.

The potency of α-, β-, γ- and δ-tocopherol in rats is 100 : 50 : 25 : 1, respectively [2, 10]. Esterification of α-tocopherol molecules reduces vitamin action by 9%. Of the tocotrienols, α-tocotrienol is the most potent; its activity is about one third of that of α-tocopherol.

Synthetic α-tocopherol is a mixture of 8 isomers and called all-rac-α-tocopherol (formerly D,L-α-tocopherol). Stable esterified forms, primarily all-rac-α-tocopherol acetate are commercially available. Its biological activity is about two thirds of that of RRR-α-tocopherol.

Digestion and absorption of tocopherols are linked to fat digestion and consequently depend on the presence of bile salts and pancreatic juice. Tocopherol esters are split in the intestine before absorption and reach the lymphatic system without being re-esterified. The absorption mechanism of tocopherols is probably based on the principle of non-saturable diffusion. The main site of absorption is the upper small intestine. The bioavailability of tocopherols largely depends on the kind of dietary fat ingested simultaneously: medium-chain saturated fatty acids favour absorption while long-chain polyunsaturated n-3 and n-6 fatty acids do not; they even inhibit absorption. Inhibition is partly also ascribed to a change in micellan structure/size and affinity to epithelial cells and to impairment of triglyceride rich lipoprotein (VLDL, LDL) synthesis by polyunsaturated fatty acids [3, 9].

Tocopherol absorption depends on the dose ingested. Given an average fat intake, 54% are absorbed from a dose of 12 mg, and 30% from a dose of 24 mg. With pharmacological doses of 200 mg, only about 10% are absorbed. Given intact biliary functions, emulsifiers such as lecithin and polysorbate may promote absorption of low doses of tocopherol. For practical purposes, an average absorption rate of 30% is assumed.

90% of absorbed tocopherol are transported in the lymph, the rest via the portal vein. 65% are taken up by LDL, 8% by VLDL and about 24% by HDL. This explains the high correlation existing between tocopherol concentration and total lipid content of the plasma. Because of its universal protective effect on membranes, vitamin E is present in all tissues. Its highest concentrations are in fatty tissue, liver and adrenal glands. There are also major quantities in the heart, skeletal muscles and testicles. In plasma, liver, kidney and spleen, tocopherol is metabolized rapidly (half-life: 5 - 7 days), but not so in fatty tissue, despite the high levels of vitamin E present there. In urine, the vitamin E metabolites α-tocopheronic acid, α-tocopheronolactone and 2, 5, 7, 8-tetramethyl-2-(2'-carboxyethyl)-6-hydroxychroman (α-CEHC) are found; α-CEHC excretion depends on plasma tocopherol concentration [5].

Because of the very close relation between vitamin E and unsaturated fatty acids, estimated values can only be set in consideration of unsaturated fatty acid intake [4, 6, 7, 13]. Calculation is based on 0.4 mg of tocopherol equivalents (TE) which are regarded as an adequate amount of vitamin E to protect 1 g of linoleic acid (diene fatty acid) [13]. To protect the double bonds in monoene, diene, triene, tetraene, pentaene and hexaene fatty acids, vitamin E quantities in the ratio of 0.3 : 2 : 3 : 4 : 5 : 6 are required [7], corresponding to 0.06; 0.4; 0.6; 0.8;

1.0; 1.2 mg TE per g of monoene fatty acids, diene fatty acids, etc.

Intakes of less than 4 mg of α-tocopherol equivalent per day, irrespective of unsaturated fatty acid intake, must be expected to considerably increase lipid peroxidation. In adults, a basic requirement of 4 mg of α-tocopherol equivalents per day has been estimated to protect double bonds formed in the body during metabolic processes against peroxidation [7]. For children and adolescents, basic requirement is interpolated according to body weight.

If the calculation is exclusively based on the recommendations or estimated values for intake of essential fatty acids plus a basic need of 4 mg TE/day, adequate daily intake for adults will be 6 - 8 mg TE.

If, however, the calculation is based on the guiding values for fat intake and the percental distribution of fatty acids (see page 39), i.e. monoene, diene and triene fatty acids included, plus a basic need of 4 mg TE/day, estimated values shown in the table will be obtained[1]. If tetraene, pentaene, hexaene acids etc. are included as well, estimated values would rise by about 0.5 mg TE.

It is possible to reach an adequate vitamin E intake without supplements, because foods with high levels of polyunsaturated fatty acids usually also contain vitamin E in appreciable amounts. In deciding what vegetable oils or margarines to buy, the vitamin E content should be an essential criterion.

An adequate intake is reflected by tocopherol concentrations in plasma and blood cells. Normal values for adults are in the range of 0.5 to 2 mg/100 ml (12 to 46 µmol/l) of plasma, or 0.8 mg/g of total lipids. A median plasma level of 30.6 ± 0.21 µmol of α-tocopherol equivalents/l was found in the VERA study. A desirable plasma level for prevention is estimated at ≥ 30 µmol/l (see section II, page 194).

Studies in older persons (> 80 years) have not shown higher tocopherol requirements than in younger adults. Digestion and absorption disorders reduce bioavailability of tocopherol and increase requirement.

Higher estimated values are set for pregnant and lactating women according to the increased requirement for energy and for unsaturated fatty acids involved.

---

[1] Example:

15 to under 19 years, female, basis 2000 kcal (table 5, page 27), 13% monounsaturated fatty acids, 7% polyunsaturated fatty acids in a ratio of 5 : 1 (see pages 39, 46) (≙ 28.9 g of oleic acid, ≙ 12.9 g of linoleic acid: ≙ 2.6 g of α-linolenic acid). By multiplication with the TE necessary per 1 g of monoene fatty acids, diene fatty acids, etc. (0.06; 0.4; 0.6 mg of TE) 8 mg of TE are obtained. Allowing for a basic requirement of 4 mg of TE, the estimate for adequate intake is 12 mg of TE/day.

As the transport of tocopherol from the placenta to the fetus is restricted, tocopherol stores in the newborn are poor. Human milk and commercial infant formulae contain enough vitamin E [11]. Self-preparation of infant formula from cow's milk is not advised, however, as the adequacy of tocopherol intake is uncertain. Estimated values for adequate intake in children of 1 - 14 years are between those for infants and adults. Starting at about the age of puberty, adult intakes are necessary.

Among the good sources of α-tocopherol are wheat-germ oil, sunflower oil, corn oil, rapeseed oil; of ß-tocopherol wheat-germ oil; of γ-tocopherol corn and soybean oil, and of δ-tocopherol soybean oil. It should be considered that part of the vitamin E content is needed to protect the oils' unsaturated fatty acids; in this function, ß- and γ-tocopherols are much more potent than in the organism. Wheat germ and hazelnuts, too, contain tocopherol in appreciable quantities. Food of animal origin contains relatively small amounts of tocopherol, depending on the way the animals were fed.

Tocopherol losses during food processing and preparation are small. In the absence of oxygen and peroxides, tocopherols are largely resistant to heat up to 200° C and to changes in pH below the neutral point. In the presence of heavy metals or rancid fats, tocopherols are rapidly oxidized by aerial oxygen. They are susceptible to daylight and UV light. In common diets and with gentle preparation, preparation losses in total food used average about 10%; major losses are caused by frying, roasting and braising [1]. Reheating frying fat destroys nearly all tocopherol still present. In deep-frozen food containing highly unsaturated fatty acids, tocopherol content decreases gradually.

Compared to the fat-soluble vitamins A and D, vitamin E is relatively non-toxic if ingested orally [8]. Oral intakes of 200 - 800 mg of α-tocopherol equivalents/day are tolerated by adults. Gastrointestinal disorders and reduced blood thyroxine levels have been found to appear occasionally after high doses. 200 mg of α-tocopherol equivalents per day are considered to be the upper limit of intake without adverse effects, particularly when acetyl salicylic acid (ASS) is concurrently taken which, like tocopherol, interferes with eicosanoid synthesis. Very high doses (> 800 mg TE/day) may inhibit platelet aggregation and thus prolong bleeding time. Therefore it is recommended to discontinue vitamin E supplementation in such amounts two weeks before and after surgical treatment.

References

[1] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[2] Elmadfa, I., Bosse, W.: Vitamin E: Eigenschaften, Wirkungsweise und therapeutische Bedeutung. Wissenschaftliche Verlagsgesellschaft, Stuttgart (1985)

[3] Elmadfa, I., Schwalbe, P.: Einige Aspekte der Bioverfügbarkeit von α-Tocopherol. Fat Sci. Techn. 91 (1989), 402-407

[4] Gaßmann, B., Kübler, W.: Ungesättigte Fettsäuren und Vitamin E-Bedarf. Ernährungs-Umschau 43 (1996), 172-177

[5] Gaßmann, B., Schulz, M., Leist, M., Brigelius-Flohè, R.: Vitamin-E-Stoffwechsel und -Bedarf. Ernährungs-Umschau 42 (1995), 80-87

[6] Horwitt, M. K.: Vitamin E and lipid metabolism in man. Am. J. Clin. Nutr. 8 (1960), 451-461

[7] Horwitt, M. K.: Status of human requirements for vitamin E. Am. J. Clin. Nutr. 27 (1974), 1182-1193

[8] Meydani, S. N., Meydani, M., Blumberg, J. B. et al: Assessment of the safety of supplementation with different amounts of vitamin E in healthy older adults. Am. J. Clin. Nutr. 68 (1998), 311-318

[9] Traber, G. M., Cohn, W., Muller, D. P. R.: Absorption, Transport and Delivery to Tissues. In: Packer, L., Fuchs, J.: Vitamin E in health and disease. Marcel Dekker, New York (1993), 35-51

[10] Schäfer, H., Elmadfa, I.: Relative bioactivity of alpha- and gamma-tocopherol calculated from respiration parameters in rat liver mitochondria. Ann. Nutr. Metab. 28 (1984), 297-304

[11] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

[12] Witting, L. A., Horwitt, M. K.: Effect of degree of fatty acid unsaturation in tocopherol deficiency-induced creatinuria. J. Nutr. 82 (1964), 19-33

[13] Witting, L. A., Lee, L.: Dietary levels of vitamin E and polyunsaturated fatty acids and plasma vitamin E. Am. J. Clin. Nutr. 28 (1975), 571-576

Vitamin K

A. Estimated values for adequate intake

Age	Vitamin K µg/day	
	m	f
Infants		
0 to under 4 months	4	
4 to under 12 months	10	
Children		
1 to under 4 years	15	
4 to under 7 years	20	
7 to under 10 years	30	
10 to under 13 years	40	
13 to under 15 years	50	
Adolescents and adults		
15 to under 19 years	70	60
19 to under 25 years	70	60
25 to under 51 years	70	60
51 to under 65 years	80	65
65 years and older	80	65
Pregnant women		60
Lactating women		60

B. Explanations

Vitamin K is a collective term comprising several compounds which may be derived from 2-methyl-1,4-naphthoquinone (menadione, vitamin K_3), a substance which has not been isolated from natural sources. Typical of vegetable vitamin K (phylloquinone, vitamin K_1) is a substituting phytyl group at the C-3 atom; typical of bacterial vitamin K (menaquinone, vitamin K_2) is a polyisoprenyl group. The latter may be composed of 4 to 13 isoprene units (each of 5 Carbon atoms). Accordingly, it is necessary to differentiate between menaquinone-4 or vitamin K_2 (20-C) and higher menaquinones or vitamin K_2 compounds. The most frequent forms are vitamin K_2 (30-C) and vitamin K_2 (35-C) with 6 and 7 isoprene units, respectively [3, 11]. Animal tissues contain phylloquinone and

menaquinone in varying ratios. The methylnaphthoquinone nucleus menadione (vitamin K_3) which has not been isolated from natural sources has no side chain. Its biological activity is explained by enzymatic alkylation of water-soluble derivatives to vitamin K_2 (20-C). The name vitamin K_3 for menadione should be avoided, and so should its use, as menadione causes considerable side effects which distinguish the compound from the actual vitamin K compounds.

The biological activity of vitamin K results from its ability to change between oxidized and reduced forms. Compounds with vitamin K action are essential for the synthesis of blood coagulation (factors II, VII, IX and X and proteins C, S and Z) [4, 12]. K vitamins, furthermore, are responsible for the biosynthesis of other proteins found in plasma, kidneys and bones (osteocalcin, a γ-carboxyglutamate-containing bone protein). Osteocalcin is probably involved in the regulation of tissue mineralization and skeletal metabolism; its synthesis in osteoblasts is partly controlled by vitamin D. Epidemiological studies have shown women aged 36 - 63 years with low vitamin K intake to be at increased risk of bone fractures [5]. This can be explained by the influence of vitamin K on osteocalcin synthesis. Established signs of vitamin K deficiency so far have only been disorders of the coagulation system, the consequences of which - visible and invisible bleedings - may occur in different organs (such as gastrointestinal tract, skin and mucosa, brain, liver, and adrenal gland).

The fat soluble K vitamins, like all fat soluble vitamins, are absorbed under the influence of bile acids and pancreatic enzymes and circulate in the plasma mainly in the LDL without needing a specific carrier. Their absorption rate of 10 - 80% may be reduced by long-chain polyunsaturated fatty acids, poorly absorbable fat soluble substances or fat substitutes. (Menadione and its water soluble derivatives, in contrast, need no bile acids for absorption (diffusion) and are transported in the blood [13]). Vitamin K_1 and vitamin K_2 are predominantly stored in the liver. (Of menadione, however, which, after conversion to menaquinone-4, is distributed to nearly every tissue, only about 2% are stored in the liver [3, 11]).

Due to insufficient placental transport of vitamin K and consequent vitamin K deficiency, haemorrhage, occasionally also intracranial, occurs in newborn and young infants. Vitamin K-deficiency haemorrhage includes early haemorrhagic disease (during the first 24 hours after birth), classic haemorrhagic disease of the newborn (during the 1^{st} week of life), and late haemorrhagic disease (during the 2^{nd} to 12^{th} week).

Vitamin K deficiency mainly occurs in exclusively breast-fed newborns. It is due to the low vitamin K content of breast milk (about 0.5 µg/100 ml) [14] and particularly to an inadequate milk supply in delayed onset of lactation. Also newborns fed commercial formulae (vitamin K content, according to EU guidelines, not less than 2.4 µg/100 ml) are at risk if they are not immediately fed on the first day of

life [1]. Prophylactic vitamin K supplementation at birth prevents bleedings observed in former times [7]. Late vitamin K-deficiency haemorrhage may also be prevented by parenteral vitamin K prophylaxis at birth. While the dose of intramuscular vitamin K prophylaxis (1 mg of vitamin K, intramuscularly) has been sufficiently verified, optimal doses of repeated oral vitamin K and the choice of preparation are still a matter of debate. In Germany, 3 x 2 mg vitamin K are recommended at present for oral vitamin K prophylaxis in healthy newborns, instead of the general parenteral vitamin K prophylaxis applied until 1992. The practice of routine intramuscular vitamin K prophylaxis was given up following reports suggesting potential carcinogenicity of intramuscular, but not of oral vitamin K prophylaxis. This suspicion could not be confirmed by any of the subsequent studies. A minimal risk for cancer could not be excluded with final certainty, however.

In adults, marginal vitamin K deficiency could be produced in experiments involving dietary restriction [16]. Vitamin K deficiency in humans has also been observed in the presence of primary diseases such as chronic hepatic diseases, gastrointestinal diseases, severe disorders of fat absorption as well as in cases of long term medication with anticoagulants, antibiotics, antiepileptics, drugs for tuberculosis or salicylates. Significant vitamin K deficiency may also occur in patients on parenteral nutrition when the infusion solution contains insufficient amounts of vitamin K and the vitamin is not otherwise supplemented. Concomitant antibiotic therapy has additional unfavourable effects.

The fact that vitamin K deficiency prolongs clotting time is clinically used for prophylaxis of thrombosis by vitamin K antagonists producing moderate vitamin K deficiency. Patients on such anticoagulant therapy should not change from a balanced to a low-vitamin K diet.

The requirements for vitamin K in man have not been precisely defined. Due to analytical problems, data on the vitamin K content of foods and thus on the average vitamin K intakes vary [8, 14]. A balanced mixed diet is supposed to supply adequate amounts of vitamin K [9]. As dietary vitamin K deficiency does not occur in healthy individuals and as in-depth experimental studies on human vitamin K requirements are not available, adequate intakes can only be estimated.

With reference to the plasma prothrombin level, an adequate daily vitamin intake of 1 µg/kg body weight has been recommended for all age groups beyond neonatal age [6, 10, 15]. Increased requirement of elderly persons has not been reported, but may occur following malabsorption or drug intake. Somewhat higher estimated values have been set for persons of advanced age as a precautionary measure. For healthy pregnant women an increased requirement is also not known. A probably very small extra need for lactating women is met by a balanced mixed diet. These statements are based on the influence of vitamin K on blood coagulation. Adequate intake of vitamin K in relation to bone metabolism has so far not been the subject of systematic investigations in humans.

Vitamin K_1 is present in rich amounts in green vegetables (30 - 800 µg/100 g). Major quantities of vitamin K compounds are also contained in milk and dairy products, muscle meat, eggs, cereals, fruit, and various other vegetables [2, 14]. Losses during food preparation are small as vitamin K is relatively insensitive to heat and oxygen. However, it is rapidly destroyed under the influence of daylight. Colonic microorganisms synthesize considerable amounts of vitamin K_2. Whether they appreciably contribute to an adequate vitamin K status is questionable.

Vitamin K toxicity is extremely low; no toxic effects are known even for phylloquinone doses in a range 500 times above the estimate.

References

[1] EG: Richtlinie der Kommission über Säuglingsanfangsnahrung und Folgenahrung vom 14. Mai 1991 (91/321/EWG), 35-49, Abl. Nr. L 175 vom 4.7.1991

[2] Elmadfa, I., Aign, W., Muskat, E., Fritzsche, D.: Die große GU Nährwert-Tabelle. Gräfe und Unzer, München (1998)

[3] Elmadfa, I., Leitzmann, C.: Ernährung des Menschen. Verlag Eugen Ulmer, Stuttgart, 3. Auflage (1998)

[4] Ferland, G.: The vitamin K-dependent proteins: an update. Nutr. Rev. 56 (1998), 223-230

[5] Feskanich, D., Weber, P., Willett, W. C., Rockett, H., Booth, S. L., Colditz, G. A.: Vitamin K-intake and hip fractures in women: a prospective study. Am. J. Clin. Nutr. 69 (1999), 74-79

[6] Frick, P. G., Riedler, G., Brogli, H.: Dose response and minimal daily requirement for vitamin K in man. J. Appl. Physiol. 23 (1967), 387-389

[7] Hansen, K. N., Ebbesen, F.: Neonatal vitamin K prophylaxis in Denmark: three years' experience with oral administration during the first three months of life compared with one oral administration at birth. Acta Paediatr. 85 (1996), 1137-1139

[8] Jakob, E., Elmadfa, I.: Application of a simplified HPLC assay for the determination of phylloquinone (vitamin K_1) in animal and plant food items. Food Chemistry 56 (1996), 87-91

[9] Jakob, E., Elmadfa, I.: Rapid HPLC assay for the assessment of vitamin K_1, A, E and beta-carotene status in children (7-19 years). Int. J. Vitam. Nutr. Res. 65 (1995), 31-35

[10] National Research Council: Recommended Dietary Allowances. 10^{th} edition, National Academy of Sciences, Washington D.C. (1989)

[11] Olson, R. E.: Vitamin K, 342-358. In: Shils, M. E., Olson, J. A., Shike, M. (eds.). Modern nutrition in health and disease. Lea & Febiger, Philadelphia, Baltimore, Hongkong, London, Munich, Sydney, Tokyo, 8^{th} edition (1994)

[12] Seegers, W. A., Watz, D. A.: Prothrombin and other vitamin K proteins. Vol. I + II, CRC Press, Boca Raton/Florida (1986)

[13] Sitrin, M. D.: Digestion and absorption of other dietary lipids, 159-186. In: Ganong, W. F. (ed.) Gastrointestinal, hepatobiliary and nutritional physiology, Lippincott-Raven, Philadelphia, New York (1996)

[14] Souci, S.W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

[15] Suttie, J. W.: Vitamin K, 137-145. In: Ziegler, E. E., Filer, L. J. jr. (eds). Present knowledge in nutrition. ILSI Press, Washington DC, 7th edition (1996)

[16] Suttie, J. W., Mummah-Schendel, L. L., Shah, D. V., Lyle, B. J., Greger, J. L.: Vitamin K deficiency from dietary vitamin K restriction in humans. Am. J. Clin. Nutr. 47 (1988), 475-480

Water-soluble vitamins

Thiamin (vitamin B_1)

A. Recommended intake

Age	Thiamin mg/day	
	m	f
Infants		
0 to under 4 months[1]	0.2	
4 to under 12 months	0.4	
Children		
1 to under 4 years	0.6	
4 to under 7 years	0.8	
7 to under 10 years	1.0	
10 to under 13 years	1.2	1.0
13 to under 15 years[2]	1.4	1.1
Adolescents and adults		
15 to under 19 years	1.3	1.0
19 to under 25 years	1.3	1.0
25 to under 51 years	1.2	1.0
51 to under 65 years	1.1	1.0
65 years and older	1.0	1.0
Pregnant women from the 4th month		1.2
Lactating women		1.4

[1] Estimated value

[2] The high value is due to thiamin requirement being related to energy intake (table 4, page 26)

B. Explanations

Thiamin acts mainly in the form of thiamin pyrophosphate, the coenzyme in important reactions in energy metabolism. Therefore it is common nutritional practice to relate thiamin requirement to energy expenditure.

Thiamin deficiency mainly causes disorders of carbohydrate metabolism. Severe thiamin deficiency leads to beriberi which, depending on its course and involvement of other nutrients, is characterized by neurological defects, wasting of skeletal muscles, cardiac insufficiency and oedema. Infantile beriberi disease occurs in breast-fed infants of women with thiamin deficiency and is manifested by sucking disorders, vomiting, apathy or restlessness, in acute courses also by life threatening cardiac insufficiency.

Absorption of the naturally occurring water-soluble vitamin via an active, carrier-mediated transport system is controlled by a saturation mechanism. The intestinal maximum concentration has been shown to be 2 µmolar (µM) [1]. At higher oral doses, a small proportion is also absorbed by diffusion; then the absorption coefficient decreases rapidly, however. In the presence of allicin, a natural component of garlic, the lipid-soluble allithiamin may already form in the intestinal tract; its absorption is a near-linear function of the dose. This also applies to gastrointestinal diseases with impaired active absorption [5].

The body's capacity for storing thiamin is low (25 - 30 mg). The biological half-life of thiamin is 10 - 20 days. A relatively regular thiamin intake is, therefore, required. High oral thiamin doses, after saturation of tissues, are rapidly excreted in the urine [4]. A suboptimal thiamin status, according to biochemical criteria (transketolase activity in erythrocytes, urinary thiamin excretion), has only been ascertained in a small sector of the population (4 - 6%) [6]. Alcoholics in particular are at high risk [1, 2].

Controlled balance studies have shown the minimum requirement for thiamin in adults to be 0.08 mg/MJ (0.33 mg/1000 kcal) [9, 11]. Following intakes of less than 0.05 mg/MJ (0.2 mg/1000 kcal), signs of deficiency appeared after 9 days in individual cases [11]. Taking the different findings into account, an amount of 0.12 mg/MJ (0.5 mg/1000 kcal) is needed by adults to ensure tissue saturation and adequate functioning of thiamin dependent enzymes. Reduced energy requirement should not lead to a thiamin intake of less than 1.0 mg per day [8]. Because requirement has been related to energy intake, nutrient density is not shown.

Because of the changed metabolic situation and fetal requirement, an additional 0.2 mg/day are needed during pregnancy. Considering an increased requirement for energy and excretion with breast milk, an allowance of 0.4 mg/day has been included for breast-feeding women [7].

In chronic alcohol abuse thiamin requirement is considerably increased due to disturbances in absorption and thiamin metabolism [1].

Good sources of thiamin are muscle meat, especially pork, liver, some fish species (plaice, tuna), whole grain products (especially oat flakes), pulses and potatoes [10].

Thiamin is readily water-soluble, sensitive to heat and oxidation, especially in neutral and alkaline media. Given common diets and gentle preparation, preparation losses in total food used average about 30% [3]. Thiamin is rapidly destroyed by sulphurous acid. Inactivation by thiaminases (e.g. in raw fish) is of no practical importance in Central Europe. In long-term chemotherapy, e.g. of cancer, thiamin supplementation is necessary.

Adverse effects of high dietary thiamin doses or high-dosed thiamin supplements (e.g. 50 - 200 mg per day) have not been reported. In individual cases, an anaphylactic reaction occurred following intravenous administration of thiamin.

References

[1] Bitsch, R.: Vitamin B_1 (Thiamin). In: Biesalski, H. K., Schrezenmeir, J., Weber, P., Weiß, H. (eds.): Vitamine - Physiologie, Pathophysiologie, Therapie. Thieme Verlag, Stuttgart-New York (1997), 67-74

[2] Bitsch, R., Hötzel, D.: Untersuchungen zur Objektivierung der Thiaminversorgung von Industriearbeitern. Akt. Ernähr. 6 (1981), 148-151

[3] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[4] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington D.C. (1998)

[5] Fujiwara, M.: Allithiamine and its properties. J. Nutr. Sci. Vitaminol. 22 (Suppl.) (1976), 57-62

[6] Kübler, W., Anders, H.-J., Heeschen, W., Kohlmeier, M. (eds.): Vitaminversorgung Erwachsener in der Bundesrepublik Deutschland. VERA-Schriftenreihe. Bd. IV, Wissenschaftlicher Fachverlag Dr. Fleck, Niederkleen (1992)

[7] Nail, P. A., Thomas, M. R., Eakin, R.: The effect of thiamin and riboflavin supplementation on the level of those vitamins in human breast milk and urine. Am. J. Clin. Nutr. 33 (1980), 198-204

[8] Nichols, H. K., Basu, T. K.: Thiamin status of the elderly: dietary intake and thiamin pyrophosphate response. J. Am. Coll. Nutr. 13 (1994), 57-61

[9] Sauberlich, H. E., Herman, Y. F., Stevens, C. O., Herman, R. H.: Thiamin requirement of the adult human. Am. J. Clin. Nutr. 32 (1979), 2237-2248

[10] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[11] Wood, B., Gijsbers, A., Goode, A., Davis, S., Mulholland, J., Breen, K.: A study of partial thiamin restriction in human volunteers. Am. J. Clin. Nutr. 33 (1980), 848-861

Riboflavin (vitamin B_2)

A. Recommended intake

Age	Riboflavin mg/day	
	m	f
Infants		
0 to under 4 months[1]	0.3	
4 to under 12 months	0.4	
Children		
1 to under 4 years	0.7	
4 to under 7 years	0.9	
7 to under 10 years	1.1	
10 to under 13 years	1.4	1.2
13 to under 15 years[2]	1.6	1.3
Adolescents and adults		
15 to under 19 years	1.5	1.2
19 to under 25 years	1.5	1.2
25 to under 51 years	1.4	1.2
51 to under 65 years	1.3	1.2
65 years and older	1.2	1.2
Pregnant women from the 4th month		1.5
Lactating women		1.6

[1] Estimated value

[2] The high value is due to riboflavin requirement being related to energy intake (table 4, page 26)

B. Explanations

Riboflavin is part of the coenzymes flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN = riboflavin phosphate) which, as part of dehydrogenases and oxidases, play a central role in oxidative metabolism. Dietary intake includes both free riboflavin and FAD and FMN. The two coenzymes are split in the proximal small intestine. Low concentrations of riboflavin are actively absorbed

following a saturation mechanism, higher concentrations by passive diffusion.

Riboflavin deficiency produces a disease which is characterized by disturbances in growth, seborrhoic dermatitis, inflammation of the oral mucosa and tongue, cracks at the corners of the mouth and, in severe cases, by normocytic anaemia. Severe riboflavin deficiency also impairs pyridoxine and niacin metabolism.

Riboflavin status is assessed by urinary riboflavin excretion in a 24-hour specimen [8] or by activation of the erythrocyte glutathione reductase (EGR) by FAD [5]. The latter may yield misleading results if the apoenzyme concentration has changed as e.g. in protein deficiency [9].

In long-term studies in adults on a diet providing 9.4 MJ/day (2200 kcal/day), a gradual increase in riboflavin intake (starting from 0.55 mg/day - a dose leading to signs of deficiency) to doses ranging from 1.1 to 1.6 mg/day resulted in an appreciable rise of 24-hour excretion, indicating that the riboflavin content of tissues was approximating saturation [8].

Studies of FAD-stimulated EGR have shown that riboflavin intakes of less than 0.11 mg/MJ (0.5 mg/1000 kcal) enhance stimulation in most of the test persons as an indication of inadequate supply; after intakes of 0.14 mg/MJ (0.6 mg/1000 kcal) FAD-stimulated EGR was in the normal range [1]. This has been taken as basis for the recommended intake [2]. A certain dependence of riboflavin requirement upon total energy expenditure is explained by the role of flavin enzymes in oxidative metabolism [12, 14]. In cases of reduced energy requirement riboflavin intake should not be less than 1.2 mg/day [4]. Because requirement has been related to energy intake, nutrient density is not shown.

During pregnancy, additional 0.3 mg of vitamin B_2 per day are recommended as reduced urinary excretion of vitamin B_2 and elevated EGR suggest higher requirement [6].

Breast milk contains 38 µg of vitamin B_2 per 100 ml on average. An allowance for lactating women of 0.4 mg/day has been derived from the vitamin B_2 content of 750 ml breast milk and a vitamin B_2 utilization rate of 70% [10, 13].

It has been shown that requirements for riboflavin increase during periods of physical activity, in cases of severe diseases after operations and trauma, in malabsorption, chronic alcohol abuse, and from interaction by various medications (e.g. antidepressives) [4, 7, 12].

Good sources of riboflavin are milk and dairy products, muscle meat, fish, eggs and whole-grain products. The riboflavin content of cow's milk is 4 times that of human milk.

In neutral and acid milieu riboflavin is poorly soluble in water and largely insensitive to heat, but inactivated by light. In food adequately stored and prepared losses of about 20% occur [3].

Adverse effects of high dietary intakes of riboflavin or high-dosed riboflavin supplements (e.g. 400 mg per day over 3 months) have not been reported [11].

References

[1] Bamji, M. S.: Glutathione reductase activity in red blood cells and riboflavin nutritional status in humans. Clin. Chem. Acta 26 (1969), 263-269

[2] Bitsch, R.: Vitamin B_2 (Riboflavin). In: Biesalski, H. K., Schrezenmeir, J., Weber, P., Weiß, H.(eds.): Vitamine - Physiologie, Pathophysiologie, Therapie. Thieme Verlag, Stuttgart-New York (1997), 75-84

[3] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernähung/nutrition 19 (1995), 411-416, 478-483, 551-554

[4] Boisvert, W. A., Mendoza, I., Castañeda, C., De Portocarrero, L., Solomons, N. W., Gershoff S. N., Russell, R. M.: Riboflavin requirement of healthy elderly humans and its relationship to macronutrient composition of the diet. J. Nutr. 123 (1993), 915-925

[5] Cooperman, J. M., Lopez, R.: Riboflavin. In: Handbook of Vitamins (Nutritional, Biochemical, and Clinical Aspects). Machlin, L. J. (ed.). Marcel Dekker Inc., New York-Basel (1984)

[6] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington D.C. (1998)

[7] Greb, A., Bitsch, R., Leinert, J., Simon-Schnaß, I.: Interaktionen zwischen Vitamin B_2 und B_6. VitaMinSpur 8 (1993), 79-80

[8] Horwitt, M. K., Harvey, C. C., Liebert, E., Steinberg, D. L.: Correlation of urinary excretion of riboflavin with dietary intake and symptoms of ariboflavinosis. J. Nutr. 41 (1950), 247-264

[9] Horwitt, M. K.: Interpretations of requirements for thiamin, riboflavin, niacin-tryptophan, and vitamin E plus comments on balance studies and vitamin B-6. Am. J. Clin. Nutr. 44 (1986), 973-985

[10] Nutrition in Pregnancy and Lactation. Report of a WHO Expert Committee. Techn. Rep. Series No. 302. WHO, Geneva (1965)

[11] Schoenen, J., Lenaerts, M., Bastings, E.: High-dose riboflavin as a prophylactic treatment of migraine: Results of an open pilot study. Cephalalgia 14 (1994), 328-329

[12] Soares, M. J., Satyanarayana, K., Bamji, M. S., Jacob, C. M., Ramana, Y. V., Rao, S. S.: The effect of exercise on the riboflavin status of adult men. Br. J. Nutr. 69 (1993), 541-551

[13] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[14] van der Beek, E. J., van Dokkum, W., Wedel, M., Schrijver, J., van den Berg, H.: Thiamin, riboflavin and vitamin B_6: Impact of restricted intake on physical performance in man. J. Am. Coll. Nutr. 13 (1994), 629-640

Niacin

A. Recommended intake

Age	Niacin mg-equivalent[1]/day m	f
Infants		
0 to under 4 months[2]	2	
4 to under 12 months	5	
Children		
1 to under 4 years	7	
4 to under 7 years	10	
7 to under 10 years	12	
10 to under 13 years	15	13
13 to under 15 years[3]	18	15
Adolescents and adults		
15 to under 19 years	17	13
19 to under 25 years	17	13
25 to under 51 years	16	13
51 to under 65 years	15	13
65 years and older	13	13
Pregnant women from the 4th month		15
Lactating women		17

[1] 1 mg of niacin equivalent = 60 mg of tryptophan

[2] Estimated value

[3] The high value is due to niacin requirement being related to energy intake (table 4, page 26)

B. Explanations

Niacin is a common term for the vitamers nicotinamide and nicotinic acid. They can be mutually converted to each other by the organism. Niacin is biochemically active in several coenzyme forms e.g. NAD (nicotinamide adenine-dinucleotide) and NADP (nicotinamide adenine-dinucleotide phosphate) which are involved in

the hydrogen-ion transfer of numerous dehydrogenases. In these biological redox reactions occurring in every cell of the organism NAD and NADP act as hydrogen donors or acceptors. Thus niacin is involved in the synthesis and degradation of carbohydrates, fatty acids and amino acids. NAD, furthermore, is involved in non-redox reactions for DNA replication and repair and for calcium mobilization [5].

Some of the free niacin is partly absorbed in the stomach, and nearly completely in the small intestine. Low niacin doses are absorbed via a sodium-dependent carrier mechanism, higher ones by passive diffusion. Even doses of several grams are well and nearly completely absorbed. In cereals, especially in maize and sorghum, niacin is largely bound to a peptide (niacytine) which is only partly digested by gastrointestinal enzymes. Alkaline hydrolysis (e.g. by lime water in the manufacture of tortilla) increases bioavailability [3].

Niacin requirement is satisfied from dietary niacin and from niacin synthesized from the essential amino acid tryptophan in the liver and kidneys. Recommendations and calculations of intake must take this into account. Tryptophan not needed for protein synthesis is either completely oxidized or used for synthesis of nicotinamide. Proteins contain on average 1% tryptophan. 60 mg of tryptophan yield about 1 mg of niacin (= 1 mg of niacin equivalent). A mixed diet composed of a wide variety of food supplying 60 g of protein contains about 600 mg of tryptophan and could provide up to 10 mg of niacin equivalents. Therefore, recommended intakes are shown in terms of niacin equivalents [4].

Every tissue is capable of synthesizing the coenzymes NAD and NADP. Tissue concentrations are controlled by extracellular nicotinamide concentrations which in turn are regulated by the liver. Surplus niacin is either stored in the liver or methylated. Methylated niacin (e.g. N^1-methyl nicotinamide) is excreted by the kidneys.

In Central Europe, niacin deficiency can only be expected to occur in cases of extreme deviations from usual dietary habits. Niacin deficiency has frequently been found in populations subsisting on maize or sorghum, the last time in an epidemic-like outbreak in African refugee camps. Inadequate supply is ascertained by reduced excretion of the niacin metabolites N^1-methyl nicotinamide and N^1-methyl-2-pyridone-5-carboxylamide and by a decrease in the NAD concentration in erythrocytes. Severe niacin deficiency in combination with low intake of tryptophan causes pellagra, a disease characterized by dermatitis (on areas of the body exposed to strong sunlight), diarrhoea, changes in the oral, glossal and gastrointestinal mucosa and by depressive psychoses with headache, fatigue and confusional states. Pellagra, if untreated, will be fatal as the entire energy metabolism is affected [1]. Chronic alcohol abuse, inborn disorders of tryptophan metabolism and chronic diarrhoea with malabsorption may also

cause deficiency. Assessing niacin supply on the basis of calculated intakes is difficult because of the varying bioavailability of niacin from tryptophan.

Following a proposal by WHO and FAO [2], recommendations for niacin intake for children and adults are calculated on the basis of energy supply: 1.6 mg/MJ (6.7 mg/1000 kcal) [6]. Reduced energy requirement should not lead to a niacin intake of less than 13 mg of niacin equivalents. Because requirement has been related to energy intake, nutrient density is not shown.

During pregnancy, more tryptophan is converted to niacin; because of the increased energy requirement (+ 1.1 MJ/day, or 255 kcal/day), however, higher niacin intake (+ 2 mg/day) is recommended.

In 750 ml of breast milk 1.3 mg of preformed niacin (plus a theoretical 2.8 mg of niacin equivalents from tryptophan with an unknown turnover rate) are secreted. This results in an allowance for lactating women of 4 mg/day. For intake in young infants an estimated value of 2 mg/day of preformed niacin has been derived.

Niacin is relatively stable during heating, cooking and prolonged storage. Preparation losses amount to less than 10% on average. Good sources of preformed niacin and tryptophan are lean meat, innards, fish, milk and eggs and, to a lesser extent, also bread and pastries, and potatoes [7]. Bioavailability of niacin from vegetable food is restricted. The high nicotinic acid content in coffee results from demethylation of trigonelline during roasting of coffee beans. Preformed niacin accounts for 50 - 60% of the total intake of niacin equivalents from a mixed diet.

High doses of nicotinic acid elicit side-effects (vasodilatation, sensation of heat, inflammation of the gastric mucosa, damage to liver cells). In adults, niacin intake with supplements should, therefore, not exceed 35 mg/day. Dietary niacin intake does not involve doses producing these side-effects. High nicotinic acid doses used for medical reasons (> 3 g per day) lower elevated levels of serum lipids, enhance utilization of muscular glycogen and reduce fatty acid mobilization in periods of physical stress [1].

References

[1] Darby, W. J., McNutt, K. W., Todhunter, E. N.: Niacin. Nutr. Rev. 33 (1975), 289-297

[2] FAO/WHO: Requirements of Vitamin A, Thiamine, Riboflavine and Niacin. FAO Food and Nutrition Series No. 8 (WHO Technical Report Series No. 362). Rome 1967, 3rd printing 1978

[3] Gaßmann, B.: Niacin. Ernährungs-Umschau 44 (1997), 384-387

[4] Horwitt, M. K., Harper, A. E., Henderson, L. M.: Niacin-tryptophan relationships for evaluating niacin equivalents. Am. J. Clin. Nutr. 34 (1981), 423-427

[5] Jacob, R. A., Svendseid, M. E.: Niacin. S. 184-190. In: Ziegler, E. E., Filer, L. J. (eds.): Present Knowledge in Nutrition. 7. Auflage, ILSI Press, Washington (1996)

[6] Moyer, E. Z., Goldsmith, G. A., Miller, O. N., Miller, J.: Metabolic patterns in preadolescent children. VII. Intake of niacin and tryptophan and excretion of niacin of tryptophan metabolites. J. Nutr. 63 (1979), 423-430

[7] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

Vitamin B_6 (pyridoxine)

A. Recommended intake

Age	Vitamin B_6 mg/day		Vitamin B_6 mg/MJ[1] (Nutrient density)	
	m	f	m	f
Infants				
0 to under 4 months[2]	0.1		0.05	0.05
4 to under 12 months	0.3		0.10	0.10
Children				
1 to under 4 years	0.4		0.09	0.09
4 to under 7 years	0.5		0.09	0.09
7 to under 10 years	0.7		0.09	0.10
10 to under 13 years	1.0		0.11	0.12
13 to under 15 years	1.4		0.13	0.15
Adolescents and adults				
15 to under 19 years	1.6	1.2	0.15	0.14
19 to under 25 years	1.5	1.2	0.14	0.15
25 to under 51 years	1.5	1.2	0.15	0.15
51 to under 65 years	1.5	1.2	0.16	0.16
65 years and older	1.4	1.2	0.17	0.17
Pregnant women				
from the 4th month		1.9		0.21
Lactating women		1.9		0.18

1 Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

2 Estimated value

B. Explanations

The term vitamin B_6 embraces a group of compounds, i.e. pyridoxine, pyridoxamine, pyridoxal, and their phosphoric esters. Pyridoxal phosphate (PLP) and pyridoxamine phosphate (PMP) act as coenzymes in more than 50 enzymatic reactions mainly in amino acid metabolism, with a prominent role in

homocysteine metabolism [9]. Vitamin B_6, furthermore, influences functions of the nervous system, immune defence and haemoglobin synthesis [7, 12].

Vitamin B_6 stores in adults last for a period of 2 - 6 weeks. The most important product excreted in the urine is 4-pyridoxic acid.

A low vitamin B_6 status is manifested by reduced urinary excretion of 4-pyridoxic acid and lowered pyridoxal phosphate concentration in blood (< 20 nmol/l) [10]. The status of vitamin B_6 is also assessed by the level of the activation coefficient of erythrocytic aspartate aminotransferase (α-EAST, previously EGOT) after *in vitro* addition of pyridoxal phosphate. An α-EAST < 2.0 suggests satisfactory intake [5]. Signs of severe vitamin B_6 deficiency are facial seborrhoic dermatitis in the region of nose, eye and mouth, anaemia not responsive to iron, and neurological symptoms (peripheral neuritis, sensory disorders, epileptiform seizures in infants).

Vitamin B_6 is mainly absorbed in the proximal jejunum by passive diffusion. The bioavailability of vitamin B_6 of vegetable origin varies greatly (0 - 80%) [4].

Healthy adults on a common mixed diet do not produce biochemical signs of deficiency if their vitamin B_6 intake is between 1.2 and 2 mg/day [8, 9]. Because of its central role in amino acid metabolism, the vitamin B_6 requirement depends on protein metabolism [5, 6, 8]. Recommendations are derived from a quotient of 0.02 mg of vitamin B_6 per g of recommended protein intake (see page 29). The values shown in the table include an allowance for variability. Where protein intake is higher than recommended, the recommended intake for vitamin B_6 also increases corresponding to the quotient specified above.

Several medications (e.g. anticonvulsants, antituberculosis drugs) increase the vitamin B_6 requirement if administered over long periods of time.

Biochemical signs of inadequate vitamin B_6 status in the last trimester of pregnancy have occasionally been reported. For pregnant women additional 0.7 mg/day are therefore recommended. An exclusively breast-feeding mother supplies on average 0.1 mg of vitamin B_6 per day. For compensation and to replenish stores an additional vitamin B_6 intake of 0.7 mg per day is advised [5].

In view of the lack of satisfactory data on infant requirement for vitamin B_6, an estimate is derived from intake with breast milk. Breast milk contains 14 µg of vitamin B_6/100 ml [11]. Usually, the recommended intake of 0.1 mg/day for the first 4 months is also achieved in infants fed commercial (fortified) infant formulae. The same applies to the recommended intake of 0.3 mg/day in infants aged 4 to under 12 months who are fed milk and supplementary food.

Vitamin B_6 is contained in nearly every food. Because of analytical problems, data on vitamin B_6 content in many foods are unsatisfactory. This reduces the accuracy of calculations of dietary vitamin B_6 intake. Good sources are e.g. poultry and pork, fish, some vegetables (cabbage family, green beans, lentils, lamb's lettuce), potatoes, bananas. Whole-grain products, wheat germ and soybeans can be recommended as well [11].

Pyridoxal is sensitive to heat and direct sunlight. Vitamin B_6 sensitivity to heat is responsible for losses during sterilization and drying of milk. Milk in transparent glass bottles exposed to sunlight will lose nearly 50% of its vitamin B_6 content within a few hours. Pyridoxine and pyridoxamine, which account for the major part of vitamin B_6 in vegetable produce, are less sensitive to heat. Given common diets and gentle preparation, preparation loss related to total food used may be up to 20% in terms of mean values [3].

Following prolonged intake of 50 - 500 mg of pyridoxine/day peripheral sensory neuropathies have been reported [1, 2]. Doses of up to 100 mg/day are regarded as safe.

References

[1] Bässler, K. H.: Megavitamin therapy with pyridoxine. Int. J. Vitam. Nutr. Res. 58 (1988), 105-118

[2] Bernstein, A. L., Lobitz, C. S.: A clinical and electrophysiologic study of the treatment of painful diabetic neuropathies with pyridoxine. In: Leklem, J. E., Reynolds, R. D., eds. Clinical and Physiological Applications of Vitamin B_6. Current Topics in Nutrition and Disease. Alan R. Liss, New York (1988)

[3] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[4] Gregory, J. F. 3rd: Bioavailability of vitamin B_6. Eur. J. Clin. Nutr. 51, Suppl. (1997), S43-S48

[5] Hansen, Ch. M., Leklem, J. E., Miller, L. T.: Change in vitamin B_6 status indication of women fed a constant protein diet with varying levels of vitamin B_6. Am. J. Clin. Nutr. 66 (1997), 1379-1387

[6] Miller, L. T., Leklem, J. E., Shultz, T. D.: The effect of dietary protein on the metabolism of vitamin B_6 in humans. J. Nutr. 115 (1985), 1663-1672

[7] Reynolds, R. D., Leklem, J. E. (eds.): Clinical and Physiological Applications of Vitamin B_6 Alan R. Liss, New York (1988)

[8] Sauberlich, H. E.: Human Requirements for Vitamin B_6. In: Vitamins and Hormons. Harris, R. S., Wool, I. G., Lorraine, J. W. (eds.). Academy Press, New York, Vol. 22 (1964), 807-823

[9] Selhub, J., Jacques, P. F., Wilson, P. W., Rush, D., Rosenberg, I. H.: Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. J. Am. Med. Assoc. 270 (1993), 2693-2698

[10] Shultz, T. D., Leklem, J. E.: Urinary 4-Pyridoxic Acid, Urinary Vitamin B_6, and Plasma Pyridoxal-Phosphate as Measures of Vitamin B_6 Status and Dietary Intakes of Adults. In: Methods in Vitamin B_6 Nutrition, Analysis and Status Assessment. Leklem, J. E., Reynolds, R. D. (eds.). Plenum Press, New York (1981), 297-320

[11] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[12] Zempleni, J.: Vitamin B_6. In: Biesalski, H. K., Schrezenmeir, J., Weber, P., Weiß, H. (eds.): Vitamine - Physiologie, Pathophysiologie, Therapie. Thieme Verlag, Stuttgart, New York (1997), 85-95

Folate / folic acid

A. Recommended intake

Age	Dietary folate		
	µg-equivalent[1]/day	µg/MJ[2] (Nutrient density)	
		m	f
Infants			
0 to under 4 months[3]	60	30	32
4 to under 12 months	80	27	28
Children			
1 to under 4 years	200	43	45
4 to under 7 years	300	47	52
7 to under 10 years	300	38	42
10 to under 13 years	400	43	47
13 to under 15 years	400	36	43
Adolescents and adults			
15 to under 19 years[4]	400	38	47
19 to under 25 years[4]	400	38	49
25 to under 51 years[4]	400	39	51
51 to under 65 years	400	43	54
65 years and older	400	48	58
Pregnant women[4]	600		65
Lactating women	600		56

[1] Calculated according to the total of compounds with folate activity in the usual diet = folate equivalents (acc. to the new definition)

[2] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[3] Estimated value

[4] Women planning a pregnancy or capable of becoming pregnant should take an additional supplement of 400 µg of synthetic folic acid (= pteryol-monoglutamic acid/PGA) to prevent neural tube defects in the infant. Supplementary folic acid intake should begin not later than 4 weeks before conception and be continued throughout the first trimester.

B. Explanations

Folate is the collective term for a family of vitamin compounds functioning as coenzymes in single-carbon transfers.

Folic acid (pteroyl-monoglutamic acid or PGA) consists of a pteridine ring and para-aminobenzoic acid, with a glutamic acid molecule bound to its carboxyl group. It is the most stable form of the vitamin with the highest degree of oxidation and is nearly completely (> 90%) absorbed. For fortification and in supplements and medications its synthetic form is exclusively used.

Folates have been defined as all dietary compounds with folate activity. Folates can have up to six glutamate residues bound to the basic molecule.

So far, activities have been expressed in terms of 'folate equivalents' to take differences of absorption into account: folate equivalent = monoglutamate + (0.2 x polyglutamate). In the Dietary Reference Intakes (DRI) of the United States [4] a new definition is used which is also applied to the present reference values: 1 µg of folate equivalent = 1 µg of dietary folate = 0.5 µg of synthetic folic acid (PGA).

In intermediary metabolism, various folate derivatives are primarily involved in processes of cell division and cell formation. Hence, folate deficiency is manifested primarily in cell systems with a high rate of cell division: red and white blood cells, intestinal and urogenital mucosa, etc. The leading effect of folate deficiency is megaloblastic anaemia. Even suboptimal folate status can frequently be ascertained by biochemical measurements. Folate metabolism is closely related to that of iron and vitamin B_{12}, a fact that should be kept in mind by those who interpret the findings of medical examination and correct a deficiency [6]. The importance of folate for homocysteine metabolism and prevention of neural tube defects will be discussed in more detail in section II, page 199.

Dietary folate is present as pteroyl-monoglutamate and pteroyl-polyglutamate. The ratio of mono-/polyglutamate may vary greatly in different foods. An average mono-/polyglutamate ratio of 50 : 50 is derived from the present dietary habits [8].

While monoglutamates are absorbed nearly completely (> 90%), only about 50% of polyglutamates are available [16] as most of them must be split by an intestinal conjugase to monglutamate compounds before absorption.

There have also been data suggesting higher bioavailability of polyglutamate compounds from investigations on single foods. It has been shown, however, that certain food components (enzyme inhibitors preventing polyglutamates from being split off, or other factors not yet known) may reduce the utilization of

folate from a mixed diet. Hence, the average bioavailability of dietary folate from a mixed diet can be reasonably estimated to be not higher than 50%.

Studies using different methods have shown that 50 - 100 µg of folic acid (in the form of synthetic pteroyl-monoglutamic acid) correct deficiency symptoms. Taking also the blood homocysteine concentration as an early indicator of inadequate folate supply into account, several studies have shown that about 400 µg of dietary folate equivalents are needed to optimally lower the homocysteine concentration. Dietary folate intakes exceeding 400 µg only influence the homocysteine concentration insignificantly [12, 14]. Hence the recommended daily intake of dietary folate is 400 µg [11, 13].

Polyglutamates account for 30% of folate in human milk and cow's milk. Folate in milk, due to its binding to protein (ß-lactoglobulin), is very well absorbed [10].

Studies in a small group of infants and small children had shown that a daily intake of 3.6 µg of total folate per kg body weight during the first year of life led to serum and erythrocyte folate concentrations near the lower limit, but not to clinical folate deficiency symptoms [1]. FAO/WHO, in 1988, called this low intake throughout the first year of life a safe level [3] and the United States even adopted it for their 1989 Recommended Dietary Allowances [9]. In their 1998 Dietary Reference Intakes the United States and Canada agreed on folate levels of 9.4 and 8.9 µg, respectively, per kg body weight as adequate intake (AI) for healthy breast-fed infants for 0 – 6 and 7 – 12 months of age [4].

As very little is known about infant requirements for folate, it seems safer to use breast milk as an orientation. An exclusively breast-fed infant (750 ml breast milk, 8 µg/100 ml) receives about 60 µg folate per day [15], in fact much more than the above mentioned minimum of 3.6 µg of total folate per kg body weight. Provided commercial infant formulae are fortified with folic acid, an increase in the estimated value for formula-fed infants seems unnecessary.

For children, experimental data on folate requirement are not available. Recommendations are estimated values based on findings in adults [1, 7]. They are set in consideration of the fact, however, that folate requirement per kg of body weight increases during growth periods due to increased formation of new cells, that it decreases with increasing age of the child and that it rises again at times of accelerated growth during puberty. The recommendations shown in the table have been set in consideration of body weight, bioavailability and requirements for growth. They have been based on folate amounts assumed to be high enough to ensure adequate folate status. Due to the high folate requirement of the fetus, pregnant women need considerably more folate. Inadequate folate supply may lead to complications during pregnancy [5]. An additional allowance of 200 µg per day is advised.

Lactating women require more folate mainly due to folate supplied with milk (80 µg/l). Taking increased demands on metabolism into account and including an extra allowance one arrives at an addition of about 100 µg of folic acid or 200 µg of dietary folate for lactating women.

Good folate sources are certain vegetables (tomatoes, cabbage, spinach, cucumbers) as well as oranges, grapes, whole grain bread and pastries, potatoes, meat, liver, milk and dairy products, some kinds of cheese, and eggs. Wheat germ and soybeans are particularly rich sources.

Folate compounds are water-soluble and sensitive to light and heat, however, with great variability among the various folate derivatives. With certain manufacturing and preparation methods, losses of up to 70% must be expected for monoglutamates and of about 50% for polyglutamates. However, more than 60% of dietary folate is supplied from food ingested raw. Hence average preparation loss could be reduced from 50 to 35% [2].

In cases of prolonged intake of certain medications (cytostatics, antiepileptics, antimalarial drugs) the organism may become depleted of folate. An influence of oral contraceptives on folate status is not verifiable anymore because newer preparations contain less oestrogen. High alcohol consumption increases the risk of folate deficiency. The contribution of enteral microbial folate synthesis to folate status is of minor importance.

Reports from the fifties have shown that high folic acid intake may mask vitamin B_{12} deficiency, as its cardinal symptom (megaloblastic anaemia) disappears while the neurological symptoms remain or get worse. So irreversible late damage of the lasting vitamin B_{12} deficiency (spinal cord degeneration) could occur. It is therefore advised to restrict a regular additional intake of folic acid to no more than 1000 µg/day, so the safe upper limit of folic acid supplementation is 1000 µg. Additional intake of dietary folate is not subject to any limit [4].

References

[1] Asfour, R., Wahbeh, N., Waslien, C. I., Guindi, S., Darby, W. J.: Folacin requirements of children. III. Normal infants. Am. J. Clin. Nutr. 30 (1977), 1098-1105

[2] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[3] FAO/WHO: Requirements of vitamin A, iron, folate and vitamin B_{12}. Report of a Joint FAO/WHO Expert Consultation. FAO Food and Nutrition Series, No. 23, FAO, Rome (1988)

[4] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington D.C. (1998), 196 – 305

[5] Hages, M., Jenke, M., Mirgel, C., Pietrzik, K.: Bedeutung einer Folsäuresubstitution während der Schwangerschaft. Geburtshilfe und Frauenheilkunde 49 (1989), 521-604

[6] Hages, M., Mirgel, C., Pietrzik, K.: Folsäure - ein kritisches Vitamin. Eine Übersicht zum aktuellen Stand der Forschung. VitaMinSpur 2 (1987), 155-169

[7] Hages, M., Pietrzik, K., Rotthauwe, H. W., Weber, H. P., von Schnakenburg, K.: Zur Folatversorgungssituation bei Kindern. Sozialpädiatrie in Praxis und Klinik 8 (1986), 23-29

[8] Müller, H.: Bestimmung der Folsäure-Gehalte von Gemüse und Obst mit Hilfe der Hochleistungsflüssigkeitschromatographie (HPLC). Z. Lebensm. Unters. Forsch. 196 (1993), 137-141

[9] National Research Council: Recommended Dietary Allowances. 10th ed., National Academy of Sciences, Washington D.C. (1989)

[10] O'Connor, D. L., Tamura, T., Picciano, M. F.: Pteroylpolyglutamates in human milk. Am. J. Clin. Nutr. 53 (1991), 930-934

[11] O'Keefe, C. A., Bailey, L. B., Thomas, E. A., Hofler, S. A., Davis, B. A., Cerda, J. J., Gregory, J. F. 3rd: Controlled dietary folate affects folate status in nonpregnant women. J. Nutr. 125 (1995), 2717-2725

[12] Pietrzik, K., Brönstrup, A.: Folate in preventive medicine; a new role in cardiovascular disease, neural tube defects and cancer. Ann. Nutr. Metab. 41 (1997), 331-343

[13] Sauberlich, H. E., Kretsch, M. J., Skala, J. H., Johnson, H. L., Taylor, P. C.: Folate requirement and metabolism in nonpregnant women. Am. J. Clin. Nutr. 46 (1987), 1016-1028

[14] Selhub, J., Jacques, P. F., Wilson, P. W., Rush, D., Rosenberg, I. H.: Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. JAMA 270 (1993), 2693-2698

[15] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

[16] Wei, M. M., Bailey, L. B., Toth, J. P., Gregory, J. F. 3rd: Bioavailability for humans of deuterium-labeled monoglutamyl and polyglutamyl folates is affected by selected foods. J. Nutr. 126 (1996), 3100-3108

Pantothenic acid

A. Estimated values for adequate intake

Age	Pantothenic acid mg/day
Infants	
0 to under 4 months	2
4 to under 12 months	3
Children	
1 to under 4 years	4
4 to under 7 years	4
7 to under 10 years	5
10 to under 13 years	5
13 to under 15 years	6
Adolescents and adults	
15 to under 19 years	6
19 to under 25 years	6
25 to under 51 years	6
51 to under 65 years	6
65 years and older	6
Pregnant women	6
Lactating women	6

B. Explanations

Pantothenic acid is involved in intermediary metabolism as an essential constituent of coenzyme A. Metabolic pathways which depend on either acetyl or acyl coenzyme A include those involved in the degradation of fats, carbohydrates and various amino acids and in the biosynthesis of fatty acids, cholesterol and steroid derivatives.

Clinical deficiency symptoms do not normally appear in humans. Evidently the minimum requirement is always satisfied. Pantothenic acid deficiency has only been reported in humans who have been fed a pantothenic acid antagonist and/or an experimental pantothenic acid-deficient diet and in individuals who

were severely malnourished due to extremely imbalanced diets, in combination with other nutritional deficits. While earlier calculations and biochemical studies arrived at a daily dietary intake of about 4 - 5 mg of pantothenic acid for German adults [7], much lower values (< 1 mg/day) have been reported more recently, part of which were derived from data of urinary pantothenic acid excretion.

Studies in adolescents showed intakes of dietary pantothenic acid to be between 4 and 7.9 mg/day [4], which did not differ from intake in adults.

Another study conducted in the United States in adolescents and young adults (age: 13 - 19 years) showed an average daily pantothenic acid intake of 4.1 mg (females) and 6.2 mg (males); it further revealed pantothenic acid pools in erythrocytes and blood which were about equally large in both sexes [2]. Average pantothenic blood levels were also in the normal range in cases with pantothenic acid intakes of less than 4 mg/day [8].

The reported intakes did not provide any indication of inadequate supply so that a daily intake of 6 mg of dietary pantothenic acid can be assumed to ensure adequate levels for adults of any age and for adolescents over 13 years.

Earlier assumptions according to which pantothenic acid deficiency may reduce the release of adrenocortical (stress) hormones have not been confirmed even in cases of severe deficiency induced in animal experiments [5]. There is no reason, accordingly, to increase intake in excess of the estimated values shown in the table either in specific stress-associated situations of life or for specific dietary habits.

An intake of 6 mg/day is also considered sufficient during pregnancy and lactation. Although pantothenic acid requirement is higher at these times, the recommended level can still be assumed to satisfy the requirement of women even under these physiological conditions. In contrast to the uniform estimated values proposed here, intakes of 5 mg for adults, of 6 mg for pregnant women and of 7 mg for lactating women have been recommended in the 1998 Dietary Reference Intakes (DRI) for the United States and Canada [3]. In view of the uncertainty of data this differentiation seems unnecessary; thus, an average intake of 6 mg/day is retained for all adults.

For children, specific data on pantothenic acid requirement are not available. Values in the tables have been interpolated from what is known about the requirements of exclusively breast-fed infants and of adolescents and adults. Breast-fed infants do not develop symptoms of pantothenic acid deficiency. An exclusively breast-fed infant receives about 1.6 mg of pantothenic acid along with its average daily portion of 750 ml breast milk.

Small quantities of pantothenic acid are contained in nearly all foods. Good sources are liver, muscle meat, fish, milk, whole-grain products and pulses (e.g. ripe peas). Pantothenic acid is water-soluble and sensitive to heat. Given customary diets and gentle preparation, preparation losses in total food used average about 30% [1].

Regular intake of even high doses of pantothenic acid is considered safe.

References

[1] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[2] Eissenstat, B. R., Wyse, B. W., Hansen, R. G.: Pantothenic acid status of adolescents. Am. J. Clin. Nutr. 44 (1986), 931-937

[3] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington D.C. (1998), 357 – 373

[4] Kathman, J. V., Kies, C.: Pantothenic acid status of free living adolescent and young adults. Nutr. Res. 4 (1984), 245-250

[5] Remer, T., Pietrzik, K.: Evidence for an increased secretory capacity for dehydroepiandrosteronesulphate in the pantothenic acid-deficient rat associated with an impaired adrenal cholesterol deposition. J. Clin. Biochem. Nutr. 7 (1989), 115-131

[6] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[7] Wagner, M., Schubert, U., Hötzel, D.: Deckung des Bedarfs an Pantothensäure bei üblichen Kostgewohnheiten. Med. Ernähr. 13 (1972), 25-29

[8] Wittwer, C. T., Schweitzer, C., Pearson, J., Song, W. O., Windham, C. T., Wyse, B. W., Hansen, R. G.: Enzymes for liberation of pantothenic acid in blood: use of plasma pantotheinase. Am. J. Clin. Nutr. 50 (1989), 1072-1078

Biotin

A. Estimated values for adequate intake

Age	Biotin µg/day
Infants	
0 to under 4 months	5
4 to under 12 months	5-10
Children	
1 to under 4 years	10-15
4 to under 7 years	10-15
7 to under 10 years	15-20
10 to under 13 years	20-30
13 to under 15 years	25-35
Adolescents and adults	
15 to under 19 years	30-60
19 to under 25 years	30-60
25 to under 51 years	30-60
51 to under 65 years	30-60
65 years and older	30-60
Pregnant women	30-60
Lactating women	30-60

B. Explanations

Biotin-dependent enzymes (carboxylases) have key functions in gluconeogenesis, in degradation of four essential amino acids (methionine, isoleucine, threonine, valine) and in the biosynthesis of fatty acids. Given common dietary habits, symptoms of biotin deficiency have so far not been observed in adults. They only occur in individuals who have ingested raw eggs in larger quantities over a prolonged period, due to avidin in egg white to which biotin is irreversibly bound. Signs of deficiency have also been found in individuals on inadequate parenteral nutrition and in children with inborn biotinidase deficiency (see below). Typical signs of deficiency are seborrhoic dermatitis, conjunctivitis, weakness, anorexia, nausea, depression and increased urinary excretion of certain organic acids,

especially 3-hydroxy-isovaleric acid. The cardinal symptom in infants is failure to thrive. There are no reliable criteria for distinguishing a deficient from a suboptimal state [2,9].

Hence the requirement for dietary biotin cannot be accurately defined. Biotin levels in breast milk vary considerably (on the average about 0.6 µg/100 ml), cow's milk contains 4 - 8 times as much [7]. An average quantity of 4.5 µg of biotin per day is ingested by infants along with an average daily intake of 750 ml breast milk [7].

Dietary biotin intakes vary greatly (< 30 µg - 150 µg/day). In a recent study most of the children and adults were found to ingest 30 - 60 µg/day [3]. Good sources are liver, soybeans, egg yolk, nuts, oat flakes, spinach, mushrooms and lentils [7]. Most dietary biotin is probably bound to protein. Little is known about the bioavailability of dietary biotin in humans [5, 6].

Release and utilization of protein-bound dietary biotin depend on the physiological enzyme biotinidase. From biocytine (ε-N-biotinyl-lysine), an intestinal proteolysis product, biotin is released either in the small intestine (pancreatic biotinidase) or, after absorption, in the intestinal mucosa or in the plasma (by plasma biotinidase) [8].

Biotinidase is even more important for the release and re-utilization of the protein-bound biotin (in holocarboxylases) in the body. Hence hereditary biotinidase deficiency leads to biotin deficiency which is associated with danger to life. Clinical symptoms including feeding problems, mental retardation, cramps, skin lesions and alopecia are prevented by early life-long oral administration of free biotin in doses of 5 - 10 mg/day [8].

High biotin doses (10 - 30 mg) have also been successful in most cases of another rare hereditary biotin-dependent enzymopathy (defective holocarboxylase synthetase) [1, 8]. Such enzyme defects may also be the cause of skin diseases occurring in infants and small children (seborrhoic dermatitis and Leiner's disease) which partly respond to biotin [4].

Re-utilization of physiological biotin may explain the fact that spontaneous signs of deficiency have rarely been observed even in individuals with extreme dietary habits. The contribution of the intestinal flora to an adequate biotin status in humans is considered negligible [2].

Hypervitaminoses of biotin are not known.

References

[1] Baumgartner, E. R., Suormala, T.: Multiple carboxylase deficiency: inherited and acquired disorders of biotin metabolism. Internat. J. Vit. Nutr. Res. 67 (1997), 377-384

[2] Bonjour, J. P.: Biotin. In: Handbook of Vitamins (Nutritional, Biochemical, and Clinical Aspects), Machlin, L. J. (ed.). 2nd edition, Marcel Dekker Inc., New York-Basel (1991), 403-435

[3] Helbich, M.: Untersuchungen zur Biotinversorgung ausgewählter Bevölkerungsgruppen. VitaMinSpur 12 (1997), 179-185

[4] Iikura, Y., Odajima, Y., Nagakura, T., Iinuma, K., Hayakawa, K., Oizumi, J.: Oral biotin treatment is effective for atopic dermatitis in children with low biotinidase activity. Acta Paediatr. Scand. 77 (1988), 762-763

[5] Krause, H. K.: Biotin. In: Biesalski, H. K., Schrezenmeir, J., Weber, P., Weiß, H. (eds). Vitamine. Physiologie, Pathophysiologie, Therapie. Thieme Verlag Stuttgart, New York (1997), 117-121

[6] Said, H. M.: Biotin bioavailability and estimated average requirement: why bother? Am. J. Clin. Nutr. 69 (1999), 352-353

[7] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[8] Wolf, B., Heard, G. S.: Disorders of Biotin Metabolism. In: The Metabolic Basis of Inherited Disease, 6th edition, Scriver, C. R., Beaudet, A. L., Sly, W. S., Valle, D. (eds.). McGraw-Hill, New York (1989), 2083-2103

[9] Zempleni, J.; Mock, D. M.: Biotin biochemistry and human requirements. J. Nutr. Biochem. 10 (1999), 128-138

Vitamin B_{12} (Cobalamins)

A. Recommended intake

Age	Vitamin B_{12}		
	µg/day	µg/MJ[1] (Nutrient density)	
		m	f
Infants			
0 to under 4 months[2]	0.4	0.20	0.21
4 to under 12 months	0.8	0.27	0.28
Children			
1 to under 4 years	1.0	0.21	0.23
4 to under 7 years	1.5	0.23	0.26
7 to under 10 years	1.8	0.22	0.25
10 to under 13 years	2.0	0.21	0.24
13 to under 15 years	3.0	0.27	0.32
Adolescents and adults			
15 to under 19 years	3.0	0.28	0.35
19 to under 25 years	3.0	0.28	0.37
25 to under 51 years	3.0	0.29	0.38
51 to under 65 years	3.0	0.33	0.41
65 years and older	3.0	0.36	0.43
Pregnant women[3]	3.5		0.38
Lactating women[4]	4.0		0.37

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Estimated value

[3] To replenish stores and to maintain nutrient density

[4] Allowance of about 0.13 µg vitamin B_{12} per 100 g of secreted milk

B. Explanations

Vitamin B_{12} (cobalamins) is a collective term for several compounds which all have a cobalt atom in the centre of a porphyrin-like ring system. Dietary or pharmaceutical cobalamins are converted by the organism to the active coenzymes adenosyl- and methylcobalamin which are involved in the intramolecular

re-arrangement of alkyl residues during degradation of odd-numbered and branched-chain fatty acids (adenosyl-cobalamin) and in the (partly folate-dependent) transfer of methyl groups (methyl-cobalamin). Thus vitamin B_{12} is required for the interconversion of the storage and transport forms of folate to its active form [2]. Only few microorganisms are capable of producing vitamin B_{12}.

Vitamin B_{12} supplied orally is absorbed in the lower small intestine only after it has formed a complex with a glycoprotein (intrinsic factor) synthesized in the gastric mucosa. Humans, therefore, are completely dependent on dietary vitamin B_{12} although large quantities are produced by the colonic microbial flora. A deficiency develops when, after resection of the stomach and in certain forms of chronic gastritis, the intrinsic factor is no longer produced or when severe inflammatory changes in the lower intestine prevent the vitamin B_{12}-intrinsic factor complex from being absorbed. However, signs of deficiency take several years to develop because body stores, mainly in the liver, normally contain 2 - 5 mg of vitamin B_{12}, of which about 0.1% per day are released. Full stores are desirable because in older individuals, malabsorption of vitamin B_{12} is more frequent than in young adults.

Advanced vitamin B_{12} deficiency, due to disturbed cell formation in bone marrow, leads to anaemia with characteristic oversized red blood cells (megaloblastic anaemia) [3]. It is partly also due to disorders of folate metabolism. Vitamin B_{12} deficiency, but not folate deficiency, may involve degeneration of certain sectors of the spinal cord (subacute combined degeneration) leading to irreversible neurological disorders.

Individual status is assessed by measurement of the plasma vitamin B_{12} concentration and of haematologic parameters [4, 7, 12]. Healthy adults need 2 µg of exogenous vitamin B_{12}. Its bioavailability decreases with increasing individual doses ingested. As more than two thirds of the total intake are supplied from main meals, it is supposed that, given the dietary habits in Central Europe, on average only 50% of the vitamin in a mixed diet is absorbed. This figure is even lower in the elderly. Hence 3 µg per day are recommended to ensure adequate intake for nearly all persons, older individuals included. Frequently more than the recommended dose of dietary vitamin B_{12} is ingested; such additional intake does not cause any harm.

During pregnancy, 0.1 - 0.2 µg per day, i.e. a total of up to about 50 µg vitamin B_{12}, are transferred to the fetus. Although a decrease in serum concentrations of vitamin B_{12} is usually observed during pregnancy, the risk of vitamin B_{12} deficiency in pregnant women and newborns is low provided adequate body stores of the vitamin were built up in earlier periods. The recommended additional vitamin B_{12} intake of 0.5 µg per day during pregnancy is a precautionary measure taken in case vitamin B_{12} stores have not been adequately filled, and to maintain

high nutrient density. The same applies to the lactation period as fully breast-feeding mothers only provide about 0.4 µg per day. A (rounded) extra of 1.0 µg per day during the lactation period allows for the daily provision of 0.4 µg in breast milk and an average absorption loss of 50% (see also footnote 4 in the table).

The estimated value of 0.4 µg per day in young infants has been derived from an average rounded quantity supplied from breast milk [10]. Breast-fed infants utilize the vitamin B_{12} content of breast milk very well. The common practice of dividing an infant's total daily food portion to 4 - 6 meals, moreover, ensures that the amount of dietary vitamin B_{12} is fully utilized. Infants, therefore, require a lower vitamin B_{12} intake (in terms of nutrient density) than adults. The recommendations for older infants and children are based on the recommendations for young infants (0.06 µg/kg body weight); they are interpolated on the basis of weight increase.

In older people, vitamin B_{12} deficiencies are more frequent than in young adults. This is due to atrophy of the gastric mucosa, possibly in combination with a vitamin B_{12} deficient diet [8, 9]. Recent data have shown that 30% of persons over 65 develop atrophic gastritis [15] which affects vitamin B_{12} absorption and reabsorption (vitamin B_{12} is largely subject to enterohepatic circulation) leading to an inadequate vitamin B_{12} status in the long run. This does not necessarily involve the classical signs of vitamin B_{12} deficiency (megaloblastic anaemia) but is manifested by disturbed enzymatic reactions. Vitamin B_{12} acts as coenzyme of methionine synthase which is needed for homocysteine metabolism [5]. Older individuals with atrophic gastritis are advised to take additional vitamin B_{12} in supplement form. Because of the atrophic gastric mucosa, the amounts of intrinsic factor are insufficient and passive vitamin B_{12} diffusion (about 1%) associated with high doses of the vitamin must be utilized; accordingly, supplementation with 100 µg is advised [14].

The richest source of vitamin B_{12} is liver; the vitamin is also present in muscle meat, fish, eggs, milk and cheese. Plant foods only contain traces of vitamin B_{12} when the food has been subject to bacterial fermentation (e.g. sauerkraut).

Common diets in Central Europe supply vitamin B_{12} in quantities considerably in excess of daily requirements. Given common diets and gentle preparation, average preparation losses in total food used are about 12% [1]. Dietary vitamin B_{12} deficiency occurs exclusively in people who have been strict vegetarians for many years, i.e. who subsist on a diet devoid of meat, dairy products and eggs. Exclusively breast-fed infants of mothers nourished that way are at increased risk for vitamin B_{12} deficiency [11, 13].

Side effects have not been observed even after very high intakes of vitamin B_{12} (pharmacological doses up to 5 mg) [6]. Consequently, supplementation including the doses recommended for elderly persons is considered safe.

References

[1] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[2] Chanarin, I.: Folate and Cobalamin. In: Haematological disorders in pregnancy. Letsky, E. A., (ed.) Clinics in Haematology 14. W. B. Saunders Company, London-Philadelphia-Toronto (1985), 629-642

[3] Chanarin, I.: The megaloblastic anemias. 3rd edition, Blackwell Scientific, Oxford (1990)

[4] Herbert, V.: Recommended dietary intakes (RDI) of vitamin B_{12} in humans. Am. J. Clin. Nutr. 45 (1987), 671-678

[5] Lindenbaum, J., Savage, D. G., Stabler, S. P., Allen, R. H.: Diagnosis of cobalamin deficiency. II. Relative sensitivities of serum cobalamin, methylmalonic acid and total homocysteine concentrations. Am. J. Hematol. 34 (1990), 99-107

[6] Martin, D. C., Francis, J., Protetch, J., Huff, J.: Time dependency of cognitive recovery with cobalamin replacement: Report of a pilot study. J. Am. Geriatr. Soc. 40 (1992), 168-172

[7] Narayanan, M. N., Dawson D. W., Lewis, M. J.: Dietary deficiency of Vitamin B_{12} is associated with low serum cobalamin levels in non-vegetarians. Eur. J. Haematol. 47 (1991), 115-118

[8] Parry, T. E.: Megaloblastic anemia in the elderly. In: Hematological Problems in the Elderly. Hamblin, T. J. (ed.), Baillière's Clinical Haematology 1. Baillière Tindall, London-Philadelphia-Toronto-Sydney-Tokyo (1987), 315-355

[9] Siurala, M., Isokoski, M., Varis, K., Kekki, M.: Prevalence of gastritis in a rural population. Bioptic study of subjects selected at random. Scand. J. Gastroenterol. 3 (1968), 211-223

[10] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[11] Specker, B. L., Black, A., Allen, L., Morrow, F.: Vitamin B_{12}: low milk concentrations are related to low serum concentrations in vegetarian women and to methylmalonic aciduria in their infants. Am. J. Clin. Nutr. 52 (1990), 1073-1076

[12] Stewart, J. S., Roberts, P. D., Hoffbrand, A. V.: Response of dietary vitamin B_{12} deficiency to physiological oral doses of cyanocobalamin. Lancet 2 (1970), 542-545

[13] Stötter, M., Mayrhofer, H.: Veganische Ernährung: Neurologische Symptomatik, schwere Entwicklungs- und Gedeihstörung bei Säuglingen und Kleinkindern durch Vitamin B_{12} - Mangel. Akt. Ernähr.-Med. 21 (1996), 4-7

[14] Ubbink, J. B., Hayward Vermaak, W. J., Van der Merve, A., Becker, P. J., Delport, R., Potgieter, C.: Vitamin requirements for the treatment of hyperhomocysteinemia in humans. J. Nutr. 124 (1994), 1927-1933

[15] Van Asselt, D. Z., de Groot, L. C., van Staveren, W. A., Blom, H. J., Wevers, R. A., Biemond, I., Hoefnagels, W. H.: Role of cobalamin intake and atrophic gastritis in mild cobalamin deficiency in older Dutch subjects. Am. J. Clin. Nutr. 68 (1998), 328-334

Vitamin C

A. Recommended intake

Age	Vitamin C		
	mg/day	mg/MJ[1] (Nutrient density)	
		m	f
Infants			
0 to under 4 months[2]	50	25	26
4 to under 12 months	55	18	19
Children			
1 to under 4 years	60	13	14
4 to under 7 years	70	11	12
7 to under 10 years	80	10	11
10 to under 13 years	90	10	11
13 to under 15 years	100	9	11
Adolescents and adults[3]			
15 to under 19 years	100	9	12
19 to under 25 years	100	9	12
25 to under 51 years	100	10	13
51 to under 65 years	100	11	14
65 years and older	100	12	14
Pregnant women from the 4th month	110		12
Lactating women[4]	150		14

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Estimated value

[3] Smokers 150 mg/day

[4] In consideration of the quantity of vitamin C secreted with 750 ml of breast milk

B. Explanations

The nutritional term vitamin C embraces several compounds of a redox system which is characterized by transfer of two electrons. It consists of L-ascorbic acid, its mono-anion ascorbate, semidehydro-L-ascorbic acid (ascorbate$^{\bullet -}$) which is

an intermediate product in free radical form, and dehydro-L-ascorbic acid. Electron transfer is reversible as long as the ring structure of dehydroascorbic acid is intact. Once it is broken hydrolytically, 2,3-dioxo-L-gulonic acid is formed and the vitamin C activity is lost.

Ascorbic acid, as electron donor, is an effective reducing agent in many intra- and extracellular reactions. The ascorbate radical has scavenger function in that it reacts with other free radicals. Biochemically, however, ascorbate is the most potent component of the redox system. Being cofactor or cosubstrate of 8 defined enzymes it influences the synthesis of collagen, carnitine and catecholamines as well as peptide amidation and tyrosine metabolism. Ascorbate reduces superoxide, hydroxyl radicals, hypochlorous acid and other reactive (pro)oxidants and is, therefore, considered to be an effective antioxidant. Intracellularly, ascorbic acid, in its electron-donor function, is involved in the interaction between iron and ferritin. Among its extracellular functions, those protecting against LDL oxidation, regenerating tocopherol from the tocopheroxyl radical and glutathione from its oxidized form are the most important. Other essential functions include reduction of dietary non-haem iron and consequent enhancement of intestinal iron absorption as well as interference with the reaction between nitrite and amines from which carcinogenic nitrosamines may emerge in the stomach. Added to these must be microsomal hydroxylation reactions needed in the liver for degradation and inactivation of medications and foreign compounds. The mechanisms of some effects, including regulation of protein translation and gene transcription are not yet understood, nor is the significance of the accumulation of ascorbate in several endocrine tissues and immunocompetent cells.

Intestinal absorption, placental transfer to the fetus, renal tubular reabsorption and accumulation in body cells are mainly accomplished by active ascorbate transport. It is dependent on concentration, sodium and energy and controlled by saturation kinetics. A second mechanism of vitamin C accumulation in body tissues is based on the transport of dehydroascorbic acid (DHA) which, upon arrival at its site of destination, is immediately reduced, in many body tissues primarily by thioltransferase (glutaredoxin). This explains why DHA escapes detection in cells and plasma. Its transport, though 10 times faster than that of ascorbate, is limited in quantity. The question of whether ascorbate and DHA are concurrently present in the intestine remains to be answered. Ascorbate probably predominates as it does in food.

The classical sign of clinical vitamin C deficiency in infants is Moeller-Barlow disease and in adults scurvy. It is manifested mainly by disturbances in bone development and growth in children and, later, by a disposition to haemorrhages in the skin, mucosa, muscles and internal organs. In industrialized countries vitamin C deficiencies are a rare occurrence. However, preclinical signs of inadequate vitamin C supply may be observed. These include general fatigue (the earliest sign),

reduced vitality, impairment of mental well-being, retarded convalescence and, not infrequently, also proneness to infectious diseases and poor wound healing.

The vitamin C status of an individual is reflected by the plasma vitamin C concentration. In the reference group of the VERA study [9] it ranged between 37 and 121 µmol/l. Values below 37 µmol/l (0.65 mg/dl) were regarded as indicative of inadequate supply. Frequently, concentrations < 20 µmol/l (0.35 mg/dl) are associated with the preclinical symptoms described before [16]. Clinical symptoms appear at ≤ 10 µmol/l (≤ 0.18 mg/dl) [9]. To reduce the risk of atherosclerosis and cancer emerging from a suboptimal antioxidant status, desirable preventive plasma levels ≥ 50 µmol/l were derived from epidemiological studies in a German consensus review [4]. With increasing vitamin C intake, plasma concentration, because of reduced absorption and increased urinary excretion, approximates a maximum value asymptotically. In a strictly controlled study, it was 80 µmol/l after oral intake of pure ascorbic acid by 7 fasting healthy non-smoking young men who had reached a steady state. Under these conditions doses of 400 - 1000 mg are necessary to achieve saturation [12]. A potential maximum body reserve of 3 g has been extrapolated from biokinetic studies.

Determination of vitamin C requirement and derivation of recommendations for dietary intake depend on the extent to which, apart from the prevention of clinical and preclinical deficiency symptoms, long-term prophylactic purposes can, and should be, pursued. This applies in the first line to strengthening the immune system and prevention of degenerative chronic diseases (atherosclerosis, cancer, cataracts, etc., see section II, page 192). Although a definitive answer cannot yet be given, the central question is about desirable body reserves and concentrations in plasma and tissue, primarily in those which are rich in vitamin C (brain, hypophysis, liver, lungs, thymus, adrenal glands, pancreas, retina, etc.). An evaluation of all epidemiological studies published before 1998 has shown that an optimal reduction of the risk for chronic diseases, especially morbidity and mortality due to cardiovascular diseases and cancer, is attained in non-smokers by plasma levels > 50 µmol/l and daily vitamin C intakes of 90 - 100 mg [6].

Hence recommended intakes aim at a desirable preventive plasma level > 50 µmol/l and saturation of immunocompetent cells (neutrophiles: 1.3 millimolar; monocytes, lymphocytes: > 3 millimolar [12, 13, 14]). Saturation to such an extent was attained in the experiment mentioned above by 100 mg of ascorbic acid per day. Under the conditions observed, pharmacokinetics followed a sigmoid course. The initially nearly linear steep increase in plasma ascorbic acid levels ceased at doses of about 100 mg; the levels attained were > 50 µmol/l.

At this plasma concentration a renal threshold becomes involved beyond which the efficacy of ascorbic acid reabsorption decreases and the concentration of

non-metabolized ascorbic acid in the urine increases. Excretion has been found to rise precipitously after intakes of 200 mg. Transport into immunocompetent cells reaches maximum speed at plasma levels of 70 µmol/l [12, 16] but is stimulated by sudden demands, e.g. in infections with fever. The VERA study [9] has shown higher plasma concentrations (20%) in women than in men. This can be taken as an advantage but not as a reason to set lower requirements and reduce recommended intakes for women.

Given 50% of maximum tissue saturation, i.e. about 1500 mg of body reserves, a plasma concentration of 50 µmol/l is associated with a metabolic turnover of about 3% corresponding to about 50 mg of vitamin C per day. Under these conditions and without further vitamin C intake it will take more than 3 weeks to reduce stores to ≤ 300 mg, a level at which clinical signs of deficiency appear. It has been calculated that daily intakes of 100 mg vitamin C should even be sufficient to maintain maximum body storage capacity of 3 g. Higher intakes raise the rate of catabolism and greatly lower elimination half-life. At intakes of 100 mg it is about 2 weeks [3].

In the VERA study [9], an average daily intake (50^{th} percentile) of 79 mg was required for non-smoking women and of 85 mg for non-smoking men to attain plasma concentrations of 50 - 75 µmol/l [11]. Assuming the bioavailability of vitamin C from a normal mixed diet to be 80% and more [16], an average requirement of 82 mg/day is derived for non-smoking adults [16]. After intake of ≤ 100 mg of pure ascorbic acid on an empty stomach, 100% of the ingested dose is bioavailable. In view of the lack of satisfactory statistical data on the variability among requirements, a coefficient of variation of 10% has been assumed. Hence the recommended intake is derived from average requirement multiplied by 1.2. The estimate for infants results from an assumed average vitamin C content in breast milk of 6.5 mg/100 ml [21] and an average daily milk intake of 750 ml (see recommendation for lactating women). Daily intakes recommended for children have been interpolated from age-related intakes for infants and those for non-smoking adults.

For pregnant women, it has been taken into account that the vitamin C plasma concentration usually decreases during pregnancy. Fetal plasma concentration is about 50% higher and the fetal ascorbic acid metabolism more intense than that of the maternal organism. The resulting decrease in maternal body reserves during pregnancy can be sufficiently countered by an allowance of 10 mg over the recommended daily intake. Provided the vitamin C requirement, per kg of body weight, for non-pregnant and pregnant women is comparable, an addition of as little as 3 - 4 mg/day is needed to satisfy fetal requirements. For assessing an additional requirement for lactating women it is assumed that 750 ml of breast milk contain about 50 mg of vitamin C.

Vitamin C requirement may be higher under some conditions of life: intense physical stress (e.g. extremely heavy manual work, high-performance sports), lasting psychic stress, alcohol and drug abuse (e.g. barbiturates, antibiotics of the tetracycline type) and some diseases, e.g. diabetes mellitus, renal insufficiency needing dialysis, and infections. The present state of knowledge does not allow for additional doses to be quantified. Heavy smokers (> 20 cigarettes per day) show decreased (about 10%) vitamin C absorption, a higher (about 40%) daily vitamin C turnover, and increased oxidative DNA damage (8-oxo-2'-desoxyguanosine) [1, 9, 17, 20]. For them, therefore, intakes of 150 mg/day are recommended. Inadequate vitamin C supply may also readily occur in older individuals who subsist on imbalanced or inadequate diets because of masticatory problems or otherwise modified conditions of life and who are dependent on sustained medication. The question of whether people of advanced age require more than 100 mg of vitamin C per day for reason of reduced absorption and to lower the risk of cataract remains to be answered [6].

In general, about 1% of non-retained ascorbic acid is converted to oxalate. Because absorption rates decrease rapidly at intakes > 200 mg and because urinary excretion of non-metabolized ascorbic acid increases accordingly, only low oxalate quantities emerge (up to 40 mg/day). Hence, healthy individuals usually are at a low risk for urinary stone formation. This is in contrast to patients with renal damage and certain subgroups of stone-formers with malabsorption who convert non-absorbed vitamin C in the gastrointestinal tract directly to oxalate which is absorbed and excreted in the urine [7]. A tolerable upper intake level for vitamin C cannot be precisely defined at present [10]. Different scientific views regarding the risk for increased renal excretion of oxalic and uric acid [16] after intake of higher vitamin C doses have been expressed; in view of some results it seems reasonable, however, to set the tolerable upper intake level for adults at 1000 mg/day as a precautionary measure. This is supported by the argument that with 1000 mg/day complete saturation of body cells and blood plasma is rapidly attained [2, 16].

The danger that ascorbic acid action changes from antioxidative to pro-oxidative is great in patients with compromised utilization of dietary iron (haemochromatosis, haemosiderosis, Cooley's anaemia) [8]. Findings of oxidative DNA changes after chronic intake of 500 mg of ascorbic acid [18] are contradictory, controversial because of the conditions and methodology employed and hence inconclusive [6, 15, 19]. If applied at very high doses (single doses of 5 g and more), ascorbic acid may cause temporary diarrhoea. So far, satisfactory scientific evidence to support the presumed effect of high-dosed vitamin C for prevention of infections is lacking.

The best vitamin C sources are fruit and vegetables and juices extracted from these. Prominent examples are sea buckthorn berries (or juice extracted from them), red and green pepper, broccoli, black currants, gooseberries, fennel and

citrus fruits [21]. Important for vitamin C supply, in terms of quantity, are also potatoes, green, red and white cabbage, Brussels sprouts, spinach, and tomatoes. Daily intakes of 200 mg are easily attained in a carefully mixed diet in which these vitamin C sources are regularly present.

Losses in the vitamin C content of fruit and vegetables by inadequate storage and culinary procedures are substantial; at worst, losses may even approximate 100%. Given common diets and gentle preparation, average losses amount to about 30% [5]. They are mainly caused by oxidation processes which could also be catalyzed by metal ions or controlled by enzymes. Vitamin C destruction is prevented by inactivation of enzymes involved (e.g. by blanching of vegetables). To preserve dietary vitamin C, those concerned with handling food and meals should make sure that oxygen and metal ions, primarily copper and iron, are excluded and that pH and temperatures are kept low.

References

[1] Asami, S., Manabe, H., Miyake, J., Tsurudome, Y., Hirano, T., Yamaguchi, R., Itoh, H., Kasai, H.: Cigarette smoking induces an increase in oxidative DNA damage, 8-hydroxydeoxyguanosine, in a central site of the human lung. Carcinogenesis 18 (1997), 1763-1766

[2] Ausman, L. M.: Criteria and recommendations for vitamin C intake. Nutr. Rev. 57 (1999), 222-224

[3] Baker, E. M., Saari, J. C., Tolbert, B. M. : Ascorbic acid metabolism in man. Am. J. Clin. Nutr. 19 (1966), 371-378

[4] Biesalski, H. K.: Antioxidative Vitamine in der Prävention. Dtsch. Ärztebl. 92 (1995), B979-B983

[5] Bognàr, A.: Vitaminverluste bei der Lagerung und Zubereitung von Lebensmitteln. ernährung/nutrition 19 (1995), 411-416, 478-483, 551-554

[6] Carr, A. C., Frei, B.: Toward a new recomended dietary allowance for vitamin C based on antioxidant and health effects in humans. Am. J. Clin. Nutr. 69 (1999), 1086-1107

[7] Gerster, H.: No contribution of ascorbic acid to renal calcium oxalate stones. Ann. Nutr. Metab. 41 (1997), 269-282

[8] Halliwell, B.: Vitamin C: antioxidant or pro-oxidant in vivo? Free Radic. Res. 25 (1996), 439-454

[9] Heseker, H., Schneider, R., Moch, K. J., Kohlmeier, M., Kübler, W.: Vitaminversorgung Erwachsener in der Bundesrepublik Deutschland, VERA-Schriftenreihe Bd. IV, Wiss. Fachverlag Dr. Fleck, Niederkleen (1992)

[10] Johnston, C. S.: Biomarkers for establishing a tolerable upper intake level for vitamin C. Nutr. Rev. 57 (1999), 71-77

[11] Kübler, W.: Zur Dosierung von Vitamin C, Vitamin E und β-Carotin mit dem Ziel der Prävention. In Hötzel, D., Walter, P. (eds.): Sauerstoff, Nutzen und Gefahren. Ganymedes Verlags- und Werbe-GmbH, Bingen (1995), 121-123

[12] Levine, M., Conry-Catilena, C., Wang, Y., Welch, R. W., Washko, P. W., Dhariwal, K. R., Park, J. B., Lazarev, A., Graumlich, J. F., King, J., Cantilena, L. R.: Vitamin C pharmacokinetics in healthy volunteers: evidence for a recommended dietary allowance. Proc. Natl. Acad. Sci. USA 93 (1996), 3704-3709

[13] Levine, M., Rumsey, S., Wang, Y.: Principles involved in formulation recommendations for vitamin C.: A paradigm for water-soluble vitamins. Methods Enzymol. 279 (1997), 43-54

[14] Levine, M., Rumsey, S. C., Wang, Y., Park, J., Kwon, O., Amano, N.: In situ kinetics: An approach to recommended intake of vitamin C. Methods Enzymol. 281 (1997), 425-437

[15] Levine, M., Daruwala, R. C., Park, J. B., Rumsey, C. R., Wang, Y.: Does vitamin C have a pro-oxidant effect? Nature 395 (1998), 231

[16] Levine, M., Rumsey, S. C., Daruwala, R., Park, J. B., Wang, Y.: Criteria and recommendations for vitamin C intake. JAMA 281 (1999), 1415-1423

[17] Loft, S., Vistisen, K., Ewertz, M., Tjonneland, A., Overvad, K., Poulsen, H. E.: Oxidative DNA damage estimated by 8-hydroxydeoxyguanosine excretion in humans: influence of smoking, gender and body mass index. Carcinogenenesis 13 (1992), 2241-2247

[18] Podmore, I. D., Griffiths, H. R., Herbert, K. E., Mistry, N., Mistry, P., Lunec, J.: Vitamin C exhibits pro-oxidant properties. Nature 392 (1998), 559

[19] Podmore, I. D., Griffiths, H. R., Herbert, K. E., Mistry, N., Mistry, P., Lunec, J.: Does vitamin C have a pro-oxidant effect? – Reply. Nature 395 (1998), 232

[20] Prieme, H., Loft, S., Klarlund, M., Gronbaek, K., Tonnesen, P., Poulsen, H. E.: Effect of smoking cessation on oxidative DNA modification estimated by 8-oxo-7,8-dihydro-2'-deoxyguanosine excretion. Carcinogenesis 19 (1998), 347-351

[21] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Aufl. medpharm Scientific Publishers, Stuttgart (2000)

Inorganic components

Inorganic components of food and the human body are grouped as follows:

Water	
Major elements	Sodium (Na), chloride (Cl), potassium (K), calcium (Ca), phosphorus (P), magnesium (Mg)
Trace elements	Iron (Fe), iodine (I), fluoride (F), zinc (Zn), selenium (Se), copper (Cu), manganese (Mn), chromium (Cr), molybdenum (Mo), cobalt (Co), nickel (Ni)
Ultratrace elements (without established physiological functions in humans so far)	Aluminium (Al), arsenic (As), boron (B), bromine (Br), cadmium (Cd), lead (Pb), rubidium (Rb), silicon (Si), samarium (Sm), titanium (Ti), barium (Ba), bismut (Bi), caesium (Cs), germanium (Ge), mercury (Hg), antimony (Sb), strontium (Sr), thallium (Tl), lithium (Li), tungsten (W)

Water

Water is the principal constituent of the human body: in adult men 60%, in adult women (with more fatty tissue) 50%, and in infants 70%. Daily total water expenditure is about 6% of body water in adults and about 20% in infants (related to total body water).

Water deficiency rapidly produces severe damage. After two to four days of deprivation the organism is no longer able to excrete substances which are liable to urinary excretion. Finally, haemoconcentration and circulatory collapse occur [1].

The data listed in table 1 refer to a total energy expenditure of 11.1 MJ (2650 kcal) under average climatic conditions in Central Europe. They are subject to changes depending on energy expenditure in individual age groups. High energy expenditure, heat, dry cold air, high intake of common salt, high protein intake and pathological states such as fever, vomiting, diarrhoea, etc. increase water requirement [2, 3].

Table 1: Water balance (ml/day) of adults[1]

Water intake		Water output	
Beverages	1440	Urine[5]	1440
Water contained in solid food[2]	875	Stool	160
Water of oxidation[3]	335	Skin	550
		Lungs	500
Total water intake[4]	2650	Total water output	2650

1 Calculated for the average of the age group 19 to under 51 years. Values were deliberately not, or little, rounded to make calculations plausible.

2 78.9 ml/MJ (0.33 ml/kcal)

3 Protein 58 g/day (9% of total energy), fat 80 g/day (27%), carbohydrates 407 g/day (63%)

4 ≈ 250 ml/MJ (1 ml/kcal)

5 Urinary volume corresponding to volume of drinks

At increased intake or increased body production of substances which are excreted in the urine as osmotically active particles (salt, urea as end product of protein degradation etc.), renal excretion is dependent on higher water intake. The lower the food intake, the higher fluid intake should be; for reduced intake of

food means reduced intake of the water contained in food, and less water of oxidation. Furthermore, there is continued accumulation of substances liable to urinary excretion.

In physical activity at high environmental temperatures, daily water requirements may be three to four times as high as those shown in the table; in extreme situations, more than 10 l per day may be needed. If water is replaced but losses of minerals (e.g. of sodium, chloride) with the water, especially by sweat, are not replaced, and if sodium is deficient as well, dilution hyponatraemia may occur (plasma sodium < 120 mmol/l), with cerebral oedema and convulsions. Fluid requirement, but not thirst, is also increased at times spent at high altitudes; this is due to the low water content of cold air inspired and to increased respiratory volume per minute in the presence of reduced oxygen pressure.

Normally, fluid intake precedes the perception of thirst under usual dietary habits. Only in exceptional cases should thirst, comparable to pain, be a stimulus for fluid intake. Especially in older individuals, however, perception of thirst may be reduced to such extent that fluid deficits are not recognized.

Due to their relatively large body surface and their still sub-maximal renal concentration capacity, infants need relatively more water than school children and adults.

The so-called water of oxidation, resulting from the combustion of nutrients ingested, is produced in quantities of 107 ml from 100 g of fat, 41 ml from 100 g of protein and 55 ml from 100 g of carbohydrates.

Renal osmolar concentration of an adult fed an average diet is about 650 mosm/day/1.73 m^2 of body surface. Optimal renal excretory functioning is associated with urinary osmolar concentrations of 500 mosm/kg. Maximal urinary concentrations in school children and adults have been found to be about 850 mosm/kg and more.

Guiding values for total water intake are about 250 ml/MJ (≈1 ml/kcal) in adults, more than 250 ml/MJ (> 1 ml/kcal) in older individuals, and about 360 ml/MJ (≈ 1.5 ml/kcal) in breast-fed infants. Breast- or formula-fed healthy infants need no additional drinks [7]. Small quantities of herbal tea may be fed to comfort the child. On transition to the family diet the child is dependent on additional fluid intake from the 10^{th} month. It should become accustomed to drinking something along with meals. Guiding values in table 2 refer to climatic conditions prevailing in Central Europe, adequate energy supply and light physical activity. If guiding values are observed, the desirable urinary volume excreted is more than 1 l and urinary osmolality about 500 mosm/kg; this is in accordance with the general rule that in adults urinary volume roughly equals the volume of fluids ingested.

Table 2: Guiding values for water intake[1]

Age	Water supplied from		Oxidation water[4]	Total water intake[5]	Water supplied from beverages and solid food
	beverages[2] ml/day	solid food[3] ml/day	ml/day	ml/day	ml/kg/day
Infants					
0 to under 4 months[6]	620	—	60	680	130
4 to under 12 months	400	500	100	1000	110
Children					
1 to under 4 years	820	350	130	1300	95
4 to under 7 years	940	480	180	1600	75
7 to under 10 years	970	600	230	1800	60
10 to under 13 years	1170	710	270	2150	50
13 to under 15 years	1330	810	310	2450	40
Adolescents and adults					
15 to under 19 years	1530	920	350	2800	40
19 to under 25 years	1470	890	340	2700	35
25 to under 51 years	1410	860	330	2600	35
51 to under 65 years	1230	740	280	2250	30
65 years and older	1310	680	260	2250	30
Pregnant women	1470	890	340	2700[7]	35
Lactating women	1710	1000	390	3100[7]	45

[1] With adequate energy supply and under average conditions (table 4, page 26). Values were deliberately not, or little, rounded to make calculations plausible.

[2] Water supplied from beverages = total water intake – oxidation water - water supplied from solid food

[3] Water supplied from solid food about 78.9 ml/MJ (≈ 0.33 ml/kcal)

[4] About 29.9 ml/MJ (≈ 0.125 ml/kcal)

[5] Breast-fed infants about 360 ml/MJ (≈ 1.5 ml/kcal), small children about 290 ml/MJ (≈ 1.2 ml/kcal), school children, young adults about 250 ml/MJ (≈ 1.0 ml/kcal), older adults about 270 ml/MJ (≈ 1.1 ml/kcal) including oxidation water (about 29.9 ml/MJ, ≈ 0.125 ml/kcal)

[6] Estimated value

[7] Rounded values

In legal terms, drinking water is regarded as food. It complies with established analytically controllable standards. The contribution of drinking water to human mineral and trace element supply varies greatly, depending on the local conditions.

Due to their particular composition some mineral waters may contribute to a selective supply of minerals and trace elements needed.

With normal drinking habits, excessive water intake is unlikely; because adults are capable of excreting nearly 1 litre per hour at times of short term stress. This volume may be considerably reduced in individuals with hepatic cirrhosis, renal insufficiency and in those dependent on diuretics [1].

Urinary volume is controlled by fluid supply to the distal tubule. Of a total glomerular filtration volume of about 170 l/day (120 ml/min/1.73 m^2 x 1440 min) 20 - 30%, or 34 - 51 l/day are transported into the distal convoluted tubule where most of it is reabsorbed. Patients suffering from diabetes insipidus have been reported to drink 35 - 41 l/day [6]. Assuming an average renal osmolar concentration of 650 mosm/day in adults and a minimum renal urinary concentration of about 50 mosm/day, one obtains a maximum urinary volume of 13 l/day as a threshold to obligatory losses of renal osmoles and development of serum hypoosmolality. Studies in volunteers who ingested excessive volumes of water at normal temperatures over several days have shown that serum osmolality is not influenced by ingested water volumes of up to 10 l per day [4]. Hence the maximum volume of fluid intake in adults that is tolerable over a prolonged period could be about 10 litres per day.

In infants and small children, acute water intoxication represents a potential risk [5, 8]. To lower serum sodium levels from 140 mmol/l to 120 mmol/l - a threshold value below which humans are at risk of cerebral oedema and convulsions - an adult of 70 kg and 42 l body water must ingest 6 l of water within a short time. A one-year-old child of 10 kg and 6.5 l needs 0.92 l and an infant of one month (4 kg, 2.8 l) 0.4 l to lower the serum sodium level below the critical threshold. Water intoxication in infants and small children has been reported to occur after renal function tests (concentration test using antidiuretic hormone analogues), gastric lavage using drinking water and after swallowing of large volumes of water in a swimming pool.

References

[1] Hierholzer, K., Fromm, M., Ebel, H.: Elektrolyt- und Wasserhaushalt. In: Pathophysiologie des Menschen. Hierholzer, K., Schmidt, R. F. (eds.), edition medizin VCH Verlagsgesellschaft, Weinheim (1991), 10.1-10.16

[2] Kuhlmann, U., Siegenthaler, G.: Wasser- und Elektrolythaushalt. In: Klinische Pathophysiologie. Siegenthaler, W. (eds.), Thieme, Stuttgart (1987), 209-224

[3] Truniger, B., Richards, P.: Wasser- und Elektrolythaushalt. Thieme, Stuttgart (1985)

[4] Habener, J. F., Dashe, A. M., Solomon, D. H.: Response of normal subjects to prolonged high fluid intake. J. Appl. Physiol. 19 (1964), 134-136

[5] Partridge, J. C., Payne, M. L., Leisgang, J. J., Randolph, J. F., Rubinstein, J. H.: Water intoxication secondary to feeding mismanagement. A preventable form of familial seizure disorder in infants. Am. J. Dis. Child. 135 (1981), 38-41

[6] Richter, C. P.: Factor determining voluntary ingestion of water in normals and in individuals with maximum diabetes insipidus. Am. J. Physiol. 122 (1938), 668-675

[7] Souci, S.W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, Medpharm, Scientific Publishers, Stuttgart (2000)

[8] Tetzner, M., Oberdisse, U.: Tödliche Wasserintoxikation nach Magenspülung mit Trinkwasser. pädiatr. prax. 40 (1990), 637-640

Minerals

Minerals is the nutritional term for those inorganic food components which, in quantities > 50 mg/day, experiments have shown to be essential in humans. Among the minerals is sulphur as part of several essential compounds such as e.g. insulin, sulphatides, keratin or glutathione peroxidase. Human requirements for sulphur are met by adequate intake of sulphur amino acids (cystine, cysteine, methionine). Sulphur, therefore, is not dealt with separately in this chapter.

Sodium, Chloride, Potassium

A. Estimated values for minimum intake

Age	Sodium[1] (mg/day)	Chloride[1] (mg/day)	Potassium[1] (mg/day)
Infants			
0 to under 4 months	100	200	400
4 to under 12 months	180	270	650
Children			
1 to under 4 years	300	450	1000
4 to under 7 years	410	620	1400
7 to under 10 years	460	690	1600
10 to under 13 years	510	770	1700
13 to under 15 years	550	830	1900
Adolescents and adults	550	830	2000

[1] 1 mmol sodium corresponds to 23.0 mg; 1 mmol chloride corresponds to 35.5 mg; 1 mmol potassium corresponds to 39.1 mg; 1 g of table salt (NaCl) consists of 17 mmol sodium and chloride each; NaCl (g) = Na (g) x 2.54; 1g NaCl = 0.4 g Na

B. Explanations

Sodium, the most abundant cation of the extracellular fluid, largely controls its volume and osmotic pressure. Sodium is also essential in the body's acid-base balance and in intestinal juices. Only a minor part of body sodium is found in the intracellular fluid where it is vitally involved in the membrane potential of cell walls and in enzyme activities. The concentration gradient between extra- and intra-

cellular sodium is maintained by an active energy consuming transport mechanism [9, 11].

Total body sodium in the newborn amounts to 5.5 g (241 mmol), in men to 100 g (4348 mmol), and in women to 77 g (3348 mmol). Per kg of body weight, newborn contain 70 mmol of sodium and adult men 60 mmol [7, 16]. Body sodium as well as sodium concentration in the extracellular fluid are primarily controlled by the aldosterone-angiotensin-renin system along with the atrial natriuretic peptide and regulated by renal mechanisms. Small quantities of sodium are excreted in the faeces.

In infants, requirement for maintenance and growth, according to balance studies and body analysis, has been estimated at 1 mmol per 100 kcal (or per 1 kg of body weight per day). This is about the sodium quantity supplied from breast milk (0.6 mmol Na/100 g or 69 kcal) [17]. In infants up to 4 months of age, because of their rapid growth, sodium retention estimated from the increase of extracellular fluid is 1.2 mmol sodium per day - the highest of all age groups. From the 5^{th} to the 12^{th} month of life, it is only 0.7 mmol/day [6].

In adults, given maximum adaptation, obligatory sodium losses were found to be about 1 mmol/day in urine plus faeces and 2 – 4 mmol/day in the skin. Sweat contains 25 mmol of sodium/l on average. As the influence of climate and physical activity may vary considerably, not less than 550 mg (24 mmol) of sodium should be ingested per day. This is equivalent to approximately 1 mmol of sodium (23 mg) per 100 kcal. During intense sweating more than 0.5 g of sodium/l sweat may be lost; the necessary intake of dietary sodium increases correspondingly [9, 15]. Sodium losses in oozing skin diseases and mucoviscidosis (typical of which are abnormally high sweat sodium concentrations) need to be replaced.

During pregnancy, because of the increase in maternal extracellular fluid, an additional requirement of 3 mmol per day has been calculated. During lactation, because of the correspondingly high sodium content of breast milk (6 mmol/l), the additional requirement amounts to 6 mmol per day [17]. These higher needs are readily met by the salt content of foods.

In adults, sodium is mainly supplied from dietary salt (NaCl). Intakes vary considerably. Under the conditions prevailing in Germany, Austria and Switzerland, 6 g of dietary salt per day are sufficient for adults. Higher intakes are not expected to yield any advantages, but could well be disadvantageous. In salt-sensitive hypertension, possibly too in people with a predisposition to this kind of hypertension, high intakes of dietary salt are injurious [4, 8, 10, 12, 13].

Studies in many countries have shown a relationship between salt intake and the incidence of high blood pressure. Depending on genetic disposition, individuals may develop hypertension in response to salt intakes typical of Western-type diets. A low-salt diet, on the other hand, has been found to lower blood pressure in many hypertensive patients [12]. A strictly low-sodium diet contains 0.4 g of sodium (or 1.0 g of table salt) per day, a low-sodium diet 1.2 g of sodium (or 3 g of table salt) per day, a moderately low-sodium diet not more than 2 g of sodium (or 5 g of table salt) per day. Sodium salts other than sodium chloride (NaCl) evidently have no substantial influence on blood pressure [13]. As well as the absolute intake of sodium chloride, the ratio of sodium to potassium intake seems to be of importance for blood pressure.

Increased urinary excretion of sodium following increased intake of table salt is associated with increased urinary excretion of calcium. In postmenopausal women elevated serum calcitriol and osteocalcin levels and higher urinary excretion of calcium and hydroxyproline after increased salt intake (from 4.1 g to 10 g/day) suggest an influence on bone metabolism [14]. In postmenopausal women, processes leading to bone loss may be intensified by high salt intake [5]. In this age group, it possibly contributes to reduced bone density [3]. For prevention of osteoporosis higher intakes of calcium are recommended (see page 141). The efficacy of this prophylactic measure should not be reduced by a high intake of table salt [3].

Chloride is the most abundant anion of the extracellular fluid. High concentrations are found in cerebrospinal fluid and in gastric juice, here in the form of hydrochloric acid. Intracellular concentrations of chloride are low [7].

Chloride plays an essential part in maintaining ion balance and acid-base equilibrium. Chloride deficiency resulting from an unusual diet or following vomiting (pylorospasm) leads to metabolic alkalosis [9].

A minimum chloride intake, in terms of molarity, largely corresponds to sodium requirement. It has been derived from the estimated values for sodium multiplied by 1.5. Increased requirement for chloride after intense sweating is also proportional to that for sodium.

In infant formulae, attention should be paid to the ratio of sodium and potassium: Breast milk contains 6 mmol sodium, 12 mmol potassium and 11.3 mmol chloride per litre [17]. The ratio between the sum of cation concentrations and the chloride concentration is (6 + 12) to 11.3 = 1.6. Infant formulae should come close to breast milk and contain these ions in a ratio of at least 1.5.

Potassium is the most abundant cation of the intracellular fluid with a concentration of 140 mmol/l. Although extracellular potassium accounts for only 2% of

the total human potassium, the human body responds very sensitively to fluctuations in extracellular potassium concentration. Both increases and decreases in extracellular potassium concentration may lead to severe neuromuscular and muscular disorders. Newborn infants contain on average 5 g (128 mmol), men 150 g (3836 mmol) and women 100 g (2558 mmol) of this mineral in their bodies. After completion of growth, the total body content of potassium is directly related to body surface (in men 2080 mmol/m^2, in women 1560 mmol/m^2) and reflects, furthermore, the metabolically active share of body mass (lean body mass, lean cellular mass) [1, 2, 7].

More than 90% of potassium ingested is absorbed in the upper small intestine. 90% is excreted by the kidneys, the rest by the bowel. Potassium excretion in sweat is negligible. The positive potassium balance prevailing in infants is supported by a high intestinal potassium absorption and a relatively low renal and colonic secretory capacity for potassium.

Adequate intake of potassium is needed to maintain electrolyte homeostasis and for growth of cellular mass (1 kg of cellular mass contains 92.5 mmol potassium). Infants during the first 4 months of life, because of their rapid growth, need 0.9 mmol/day for development of cellular mass; boys and girls up to 12 years need 0.4 - 0.5 mmol/day. For the period of accelerated growth in puberty, 0.9 mmol/day are required [6]. The requirement for maintaining homeostasis is estimated on the basis of total energy intake which, in turn, should be proportional to cell mass and, thus, the body's total potassium content. In infants, nearly 2 mmol potassium are set for 100 kcal, corresponding to the energy and potassium content of breast milk (table IV, page 209) [17]. Less than 10% of the total requirement for potassium is spent on growth. During pregnancy and lactation, there is no appreciable additional requirement for potassium.

Adults ingest 50 - 75 mmol per day corresponding to 2 - 3 g of potassium or 2 - 3 mmol/100 kcal from common diets in Central Europe. This is sufficient under normal conditions. High intakes of potassium have been found to reduce blood pressure.

High losses of potassium, e.g. in cases of severe diarrhoea or vomiting, must be compensated for by increased intake. Higher amounts of potassium may also be required by individuals taking laxatives and diuretics [9].

As the kidneys continue excreting potassium even in states of depletion, signs of deficiency may rapidly occur if dietary intake is insufficient. Typical signs of potassium deficiency are neuromuscular symptoms such as weakness of skeletal muscles, relaxation of smooth muscles, ileus and cardiac dysfunction. Patients with renal insufficiency and inadequate potassium excretion are at risk for potassium intoxication especially when potassium-saving diuretics are taken

in addition. Increased blood potassium concentrations then affect cardiac functions.

The potassium content of usual food and particulary of food of vegetable origin (bananas, potatoes, dried fruit, spinach, mushrooms) is sufficient due to its high intracellular potassium concentrations. The potassium content of food decreases during cooking due to transfer of potassium into the cooking medium.

References

[1] Aizman, R.; Grahnquist, L.; Celsi, G.: Potassium homeostasis: ontogenic aspects. Acta Paediatr. 87 (1998), 609-617

[2] Burmeister, W., Bingert, A.: Die quantitativen Veränderungen der menschlichen Zellmasse zwischen dem 8. und 90. Lebensjahr. Klin. Wschr. 45 (1967), 409-416

[3] Devine, A., Criddle, R. A., Dick, I. M., Kerr, D. A., Prince, R. L.: A longitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. Am. J. Clin. Nutr. 62 (1995), 740-745

[4] Die Intersalt-Forschungsgruppe aus BRD und DDR: Blutdruck, relatives Körpergewicht, Alkoholkonsum und Elektrolytausscheidung in der BRD und der DDR: Die Intersalt-Studie. Klin. Wochenschr. 68 (1990), 655-663

[5] Evans, C. E., Chughtai, A. Y., Bluhmsohn, A., Giles, M., Eastell, R.: The effect of dietary sodium on calcium metabolism in premenopausal and postmenopausal women. Eur. J. Clin. Nutr. 51 (1997), 394-399

[6] Fomon, S., J.: Nutrition of normal infants. Mosby, St. Louis (1993)

[7] Forbes, G. B.: Human Body Composition. Growth, Aging, Nutrition and Activity. Springer, Berlin-Heidelberg-New York (1987), 144-146, 170, 180

[8] Gleichmann, U.: 1. Consensuskonferenz der Deutschen Akademie für Ernährungsmedizin: Stellenwert der Kochsalzreduktion in der Prävention und Behandlung der Hypertonie. Akt. Ernähr.-Med. 19 (1994), 40-41

[9] Hierholzer, K., Fromm, M., Ebei, H.: Elektrolyt- und Wasserhaushalt. In: Pathophysiologie des Menschen. Hierholzer, K., Schmidt, R. F. (eds.). edition medizin, VCH Verlagsgesellschaft, Weinheim (1991), 10.1-10.16

[10] Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. Intersalt Cooperative Research Group. BMJ 297 (1988), 319-328

[11] Kumar, S.; Berl, T.: Sodium. Lancet 352 (1998), 220-228

[12] Law, M. R., Frost, C. D., Wald, N. J.: By how much does dietary salt reduction lower blood pressure? I: Analysis of observational data among populations. II: Analysis of observational data within populations. III: Analysis of data from trials of salt reduction. BMJ 302 (1991), 811-824

[13] Luft, F., Ganten, D.: Salz ist nicht gleich Salz. Dtsch. Med. Wschr. 112 (1987), 1391-1394

[14] McParland, B. E., Goulding, A., Campbell, A. J.: Dietary salt affects biochemical markers of resorption and formation of bone in elderly women. BMJ 299 (1989), 834-835

[15] National Research Council: Recommended Dietary Allowances. 10th edition, National Academy of Sciences, Washington D.C. (1989)

[16] Romahn, A., Burmeister, W.: Die Körperzusammensetzung während der ersten zwei Lebensjahre. Bestimmungen mit der Kalium 40-Methode. Klin. Pädiat. 189 (1977), 321-327

[17] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

Calcium

A. Recommended intake

Age	Calcium		
	mg/day	mg/MJ[1] (Nutrient density)	
		m	f
Infants			
0 to under 4 months[2]	220	110	116
4 to under 12 months[2]	400	133	138
Children			
1 to under 4 years	600	128	136
4 to under 7 years	700	109	121
7 to under 10 years	900	114	127
10 to under 13 years	1100	117	129
13 to under 15 years	1200	107	128
Adolescents and adults			
15 to under 19 years	1200	113	141
19 to under 25 years	1000	94	123
25 to under 51 years	1000	98	128
51 to under 65 years	1000	109	135
65 years and older	1000	120	145
Pregnant women[3]	1000		109
Lactating women[4]	1000		93

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Estimated value

[3] Pregnant women under 19 years 1200 mg

[4] Lactating women under 19 years 1200 mg

B. Explanations

Calcium ions are essential for cellular life. They are vitally involved in the stabilization of cell membranes, intracellular signal transmission, stimulus transfer in the nervous system, electromechanical coupling in muscles and blood coagulation. In vertebrates, calcium salts stabilize firm substances (bones for load-carrying

capacity and protection of organs, teeth for size-reduction of food). Bone tissue is at the same time an important calcium store for times of shortage.

The body of newborn infants contains about 25 - 30 g of calcium, that of adult men 900 - 1300 g, that of women 750 - 1100 g [15]. More than 99% of the calcium is located in the skeleton and teeth. Calcium retention for bone development results from the difference between the quantities of calcium ingested and those excreted in faeces, urine and via the skin.

During the first 5 - 6 years of life, about 100 mg of calcium are retained per day for bone development. During the period of accelerated growth during puberty up to 400 mg and more may be retained per day. The calcium absorption rate decreases after adolescence; in young adults, not more than 150 mg per day are retained.

Calcium absorption is enhanced by vitamin D and is dependent on calcium supply. There has been no satisfactory evidence for lactose promoting status calcium absorption. Given common dietary habits, the inhibiting effect of food components such as oxalates, phytates, lignins and uronic acids on the bioavailability of calcium is of little practical importance. In infants, as much as 75% of calcium ingested may be absorbed. In adults, this figure amounts to 20 - 40%; the range of variability is 10 - 60% [4]. The calcium absorption rate decreases with increasing age [3]. Dietary salt and proteins containing a high proportion of sulphur amino acids (animal protein in particular) increase calcium excretion; this increase is dose-dependent (see page 33, 135).

Next to infants' age, puberty is characterized by very intense bone growth. By the end of adolescence, 90% of peak bone mass is achieved. In girls, in whom puberty begins earlier, this point is reached about two years earlier than in boys [12]. Bone development is completed in the 3rd decade of life. During the 4th decade of life bone mass begins to decline and the decrease accelerates in menopausal women, in whom it may lead to osteoporosis. This process is retarded by oestrogen replacement and increased physical activity. In older men, due to a less abrupt decrease in the production of sex hormones and continued presence of higher muscle mass, bone loss is less than in women. Also older individuals are still capable of increasing bone mass.

Prophylactic measures to prevent osteoporosis essentially aim at optimizing peak bone mass in the young and minimizing bone loss in the elderly. Failure to achieve these goals by higher calcium intake from a mixed diet does not furnish sufficient reason to recommend calcium supplements and calcium-fortified food. Adequate hormonal status and physical activity are as important as is sufficient calcium intake. Elderly women must also ensure adequate protein intake (see page 33) [9].

An exclusively breast-fed infant receives about 220 mg of calcium from 750 ml of breast milk (absorption rate about 67%) [13]. For infants fed commercial formulae and, later, supplementary food calcium requirement has been estimated at 400 mg/day; an absorption rate of < 50% of calcium from cow's milk products has been taken into account.

For the optimal level of calcium intake an age-related threshold has been reported [7]. Intakes exceeding this value do not appreciably improve calcium balance or the mineral content of bones. Excess calcium is excreted in faeces and, to a lesser extent, in urine.

The results of calcium balance studies are reason to assume a plateau of calcium retention at an intake of about 1500 mg/day during puberty [11]. In intervention studies, calcium intakes exceeding an average of 1000 mg/day produced a higher mineralization of bones than average intakes of 728 and 935 mg of calcium/day [1, 6]. Calculations allowing for daily obligatory renal, dermal and endogenous faecal calcium losses and including the intestinal calcium absorption rate and the necessary calcium retention suggest that during puberty and adolescence 1000 – 1500 mg/day of dietary calcium are needed. Because there is no satisfactory evidence for the preventive use of very high calcium intakes [2], the recommended intake has been set at 1200 mg/day. In young adults, an adequate balance is achieved by 500 - 600 mg/day [11]; however, for maximum calcium retention and maximum mineralization of bones about 900 mg/day are needed [5, 7]. Accordingly, and in consideration of the variability among calcium requirements, the recommended intake for adults is set at 1000 mg/day.

The postmenopausal loss of bone mass cannot be stopped by increased calcium intake. However, the effect of oestrogen intake on calcium retention is potentiated by high calcium doses [10]. The optimal daily calcium dose for elderly individuals is not known. The requirement for dietary calcium of men and women over 50 years is probably greater than that of younger adults. 1000 mg/day should be adequate also for this age group, however.

During pregnancy, women must provide about 25 - 30 g of calcium and another 50 g for 4 - 6 months of breast-feeding and subsequent gradual weaning. During pregnancy, both calcium absorption rate and renal calcium losses increase. There is no evidence for calcium storage in the maternal organism. High calcium intakes during lactation cannot stop bone mineral loss caused by hormonal changes (hypoestrogenaemia). However, a higher number of pregnancies and prolonged lactation periods do not put the mother at risk of osteoporosis; the temporary loss of bone mass is repaired by hormonal adaptation mechanisms after weaning [14].

Milk and dairy products are good calcium sources for every age. Low-fat milk and dairy products of low-fat milk should be preferred. Also subjects with lactose intolerance are usually able to eat certain dairy products such as yoghurt and ripe cheeses without abdominal complaints. Some vegetables (e.g. broccoli, green cabbage, fennel, leak) and some mineral waters (> 150 mg calcium/l) may contribute towards an adequate calcium supply. Calcium should be ingested with several meals over the day and especially with a calcium-containing late meal in the evening; this will reduce nightly processes of bone demineralization. The recommended intakes can be realized with a balanced mixed diet, adequate energy supply provided.

In urinary stone formers, a high calcium intake may influence the risk for urinary stones differently, depending on the conditions of the individual case. Even though the development of urinary calcium stones may be promoted, high calcium intakes may also bind dietary oxalic acid in the intestine and, by reduced urinary oxalate uptake and excretion, contribute to an enhanced urinary solubility product [8]. Individuals at risk for urinary stones should not exceed the doses recommended and ensure an adequate urinary volume. Interactions between calcium and other cations such as magnesium, iron and zinc as well as phosphorus have been reported. However, following high calcium intakes there are no indications of functional disorders of metabolic processes for which the nutrients mentioned before are essential. Nor has there been any scientific evidence for the influence of increased calcium doses of up to 2 g per day on the development of atherosclerosis in humans. Calcium intakes of several grams per day especially in combination with high alkali intakes may elicit hypercalcaemia and lead to calcium deposits in soft tissues, especially in the kidneys (milk-alkali syndrome). In well documented cases calcium intake was > 4 g/day [16]. In some of these, however, only the calcium supply from supplements, but not from additional dietary intake was taken into account. In healthy adults with a urinary volume of > 2 l/day a calcium intake of up to 2 g/day is considered to be safe.

References

[1] Chan, G. M., Hoffman, K., McMurry, M.: Effects of dairy products on bone and body composition in pubertal girls. J. Pediatr. 126 (1995), 551-556

[2] Fehily, A. M., Coles, R. J., Evans, W. D., Elwood, P. C.: Factors affecting bone density in young adults. Am. J. Clin. Nutr. 56 (1992), 579-586

[3] Heaney, R. P., Recker, R. R., Stegman, M. R., Moy, A. J.: Calcium absorption in women: relationship to calcium intake, estrogen status, and age. J. Bone Min. Res. 4 (1989), 469-475

[4] Heaney, R. P., Recker, R. R.: Distribution of calcium absorption in middle-aged women. Am. J. Clin. Nutr. 43 (1986), 299-305

[5] Kanders, B., Dempster, D. W., Lindsay, R.: Interaction of calcium nutrition and physical activity on bone mass in young women. J. Bone Min. Res. 3 (1988), 145-149

[6] Lloyd, T., Andon, M. B., Rollings, N., Martel, J. K., Landis, J. R., Demers, L. M., Eggli, D. F., Kieselhorst, K., Kulin, H. E.: Calcium supplementation and bone mineral density in adolescent girls. JAMA 270 (1993), 841-844

[7] Matkovic, V., Heaney, R. P.: Calcium balance during human growth: evidence for threshold behavior. Am. J. Clin. Nutr. 55 (1992), 992-996

[8] Massey, L. K., Roman-Smith, H., Sutton, R. A.: Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. J. Am. Diet. Assoc. 39 (1999), 901-906

[9] Munger, R. G., Cerhan, J. R., Chin, B. C.: Prospective study of dietary protein intake and risk of hip fracture in postmenopausal women. Am. J. Clin. Nutr. 69 (1999), 147-152

[10] Nieves, J. W., Komar, L., Cosman, F., Lindsay, R.: Calcium potentiates the effect of estrogen and calcitonin on bone mass: review and analysis. Am. J. Clin. Nutr. 67 (1998), 18-24

[11] Nordin, B. E., Polley, K. J., Need, A. G., Morris, H. A., Marxhall, D. H.: The problem of calcium requirement. Am. J. Clin. Nutr. 45 (1987), 1295-1304

[12] Peacock, M.: Calcium absorption efficiency and calcium requirements in children and adolescents. Am. J. Clin. Nutr. 54 (1991), 261S-265S

[13] Souci, S., Fachmann, W., Kraut, W.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[14] Sowers, M., Corton, G., Shapiro, B., Jannausch, M. L., Crutchfield, M., Smith, M. L., Randolph, J. F., Hollis, B.: Changes in bone density with lactation. JAMA 269 (1993), 3130-3135

[15] Weaver, C. M., Peacock, M., Martin, B. R., Plawecki, K. L., McGabe, G. P.: Calcium retention estimated from indicators of skeletal status in adolescent girls and young women. Am. J. Clin. Nutr. 64 (1996), 67-70

[16] Whiting, S.J., Wood, R.J.: Adverse effects of high-calcium diets in humans. Nutr. Rev. 55 (1997), 1-9

Phosphorus

A. Recommended intake

Age	Phosphorus mg/day
Infants	
0 to under 4 months[1]	120
4 to under 12 months	300
Children	
1 to under 4 years	500
4 to under 7 years	600
7 to under 10 years	800
10 to under 13 years	1250
13 to under 15 years	1250
Adolescents and adults	
15 to under 19 years	1250
19 to under 25 years	700
25 to under 51 years	700
51 to under 65 years	700
65 years and older	700
Pregnant women[2]	800
Lactating women[3]	900

[1] Estimated value

[2] Pregnant women under 19 years 1250 mg

[3] Lactating women under 19 years 1250 mg

B. Explanations

Organic phosphorus compounds are part of membranes and nucleic acid occurring in all living cells. Many cellular metabolic processes are controlled by phosphorylation reactions. Inorganic phosphates have buffering activity in maintaining pH.

The body of newborn infants contains about 17 g of phosphorus, that of adults about 600 - 700 g. More than 85% of the total phosphorus is located in the

skeleton and teeth, about 65 - 80 g are found in the remaining tissues and only about 2 g in the blood.

In breast-fed infants, up to 90% of ingested phosphorus is absorbed. Adults absorb 55 - 70% from a mixed diet mainly by facilitated diffusion and to a lesser extent by an active process involving vitamin D. The bioavailability of phosphorus from plant seeds is low. In the latter, phosphorus bound in phytic acid can be released by microbial phytase (e.g. during manufacture of bread).

Phosphorus forms an insoluble compound with aluminium. Aluminium compounds previously used for treatment of renal insufficiency have, therefore, largely been replaced by calcium carbonate.

Serum phosphate levels depend on age, renal excretory capacity and dietary phosphorus intake. A renal threshold for phosphorus (maximum phosphate transport/glomerular filtration rate) regulates serum phosphate concentration and homeostasis [5]. The relatively high serum phosphate concentrations in infants, small children and school children promote skeletal mineralization. In adults, the phosphate quantity daily excreted in the kidneys reflects the quantity absorbed from food [6].

In breast-fed infants phosphorus is the limiting element of skeletal mineralization. The low concentration of phosphorus in breast milk [7] corresponds to the infant's relatively low renal capacity for excreting in particular phosphate. In breast-fed infants, furthermore, only small quantities of the strongly buffering phosphate reach the lower intestinal sections; the resulting low pH promotes the growth of fermentation bacteria which protect the infant against infections [4].

While in the previous edition DGE had specified obligatory levels for phosphorus intake, now recommendations are made which, by definition, are distinctly lower. Data from which recommended intakes could be derived are much rarer for phosphorus than for calcium. Average requirement for adults has been estimated at 580 mg/day [2]. Given a coefficient of variation of 10%, the recommended intake will be 700 mg/day including an extra allowance of 20%. At the age of puberty and adolescence, the requirement for phosphorus is increased because of new tissue formation and bone growth in particular. Accordingly, the recommended intake is increased to 1250 mg/day. During pregnancy, an average of 60 mg extra phosphorus and during lactation of 90 - 120 mg per day must be provided. Allowances of 100 mg/day for the duration of pregnancy and of 200 mg/day for the lactation period have been fixed bearing in mind the intestinal absorption rate.

Phosphorus deficiency caused by dietary inadequacy has not been reported, for almost all foods contain phosphorus. Intakes, therefore, are not shown in

terms of nutrient density. Symptoms of deficiency which only appear in subjects on parenteral nutrition with inadequate phosphorus content [3] include hypophosphataemia and general physical weakness. A diet deficient in phosphorus is also deficient in protein and calcium.

Intakes of 1.5 to 2.5 g of phosphorus lower serum calcium levels and raise serum concentrations of parathyroid hormone. This does not affect calcium balance, in contrast to earlier assumptions, or intensify processes involved in bone loss [1, 8]. There is no need, according to present knowledge, to observe a particular Ca : P ratio in the diet.

Ortho- and polyphosphates added to food in compliance with legal regulations are harmless. Subjects with compromised renal function are at risk for phosphorus intoxication, with hyperphosphataemia and renal calcification. In healthy individuals, phosphorus intoxication following excessive dietary intakes have not been reported. The upper limit for physiological serum phosphate concentrations in adults would be reached after an intake of 3.5 g of phosphorus per day. This limit is exceeded after intake of certain medications (e.g. bisphosphonates); however, intoxications have not been reported.

References

[1] Bizek, B. K., Ding, W., Cerklewski, F. L.: Evidence that bone resorption of young men is not increased by high dietary phosphorus obtained from milk and cheese. Nutr. Res. 16 (1996), 1143-1146

[2] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy Press, Washington D.C. (1997), 146-189

[3] Knochel, J. P.: The pathophysiology and clinical characteristics of severe hypophosphatemia. Arch. Intern. Med. 137 (1977), 203-220

[4] Manz, F.: Why is the phosphorus content of human milk exceptionally low? Monatsschr. Kinderheilkd. 140 (1992), S35-S39

[5] Robertson, W. G.: Plasma phosphate homeostasis. In: Calcium, phosphate and magnesium metabolism. Ed.: BEC Nordin. Churchill Livingstone, Edinburgh (1976), 217-229

[6] Robertson, W. G.: Urinary excretion. In: Calcium, phosphate and magnesium metabolism. Ed.: BEC Nordin. Churchill Livingstone, Edinburgh (1976), 113-161

[7] Souci, S., Fachmann, W., Kraut, W.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[8] Spencer, H., Kramer, L., Osis, D.: Do protein and phosphorus cause calcium loss? J. Nutr. 118 (1988), 657-660

Magnesium

A. Recommended intake

Age	Magnesium			
	mg/day		mg/MJ[1] (Nutrient density)	
	m	f	m	f
Infants				
0 to under 4 months[2]	24		12	13
4 to under 12 months	60		20	21
Children				
1 to under 4 years	80		17	18
4 to under 7 years	120		19	21
7 to under 10 years	170		22	24
10 to under 13 years	230	250	24	29
13 to under 15 years	310	310	28	33
Adolescents and adults				
15 to under 19 years	400	350	38	41
19 to under 25 years	400	310	38	38
25 to under 51 years	350	300	34	38
51 to under 65 years	350	300	38	41
65 years and older	350	300	42	43
Pregnant women[3]		310		34
Lactating women		390		36

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Estimated value

[3] Pregnant women under 19 years 350 mg

B. Explanations

Magnesium is the fourth most common cation in the human body. 60% of the body's magnesium is found in the skeleton, 30% in muscles, 1% in the extracellular fluid, the rest intracellular. Newborns contain 0.7 g of magnesium, 5-year-old children 5 g and adults about 25 g. Magnesium activates several enzymes

(especially those involved in energy metabolism), acts as cofactor of phosphorylated nucleotides and contributes to nucleic acid synthesis. In the field of bone mineralization and membrane physiology magnesium plays an essential part in the synaptic neuromuscular stimulus transfer and in muscular contraction.

Magnesium deficiency with defined symptoms has so far not been verified in healthy humans with common dietary and lifestyle habits. In the presence of gastrointestinal diseases, especially chronic malabsorption and in chronic alcohol abuse, magnesium supply may however be insufficient. The same applies to the chronic intake of certain medications (e.g. diuretics, corticoids, oral contraceptives). Severe magnesium deficiency leads to dysfunctioning of cardiac and skeletal muscles, muscular weakness and disposition to muscle cramps.

20 - 30% of dietary magnesium is absorbed by active transport and free diffusion [7, 8]. Absorption is influenced by the quantity of magnesium supplied, solubility of the magnesium salt and the amounts of dietary phytate, fibre, calcium and long-chain triglycerides ingested [10]. Magnesium ingested in excess is primarily excreted via the kidneys. Excretion is regulated in the renal tubules. Parathyroid hormone and vitamin D act both directly and indirectly on the blood magnesium concentration; the regulating mechanism is not yet precisely known, however.

In Germany, the average daily magnesium intake from a mixed diet is about 280 mg in women and 350 mg in men [1]. Balance studies have shown the average requirement for magnesium for young adult men to be 330 mg per day. Accordingly, the Dietary Reference Intakes (DRI) of the United States recommend 400 mg per day for men (19 - 30 years). For young women (19 - 30 years) average requirement is 255 mg and the recommended dietary allowance (RDA) 310 mg per day [2].

The intakes recommended in the table are based on many balance studies [2, 3, 4, 5, 6, 11]. They are in agreement with those recommended by other countries with similar dietary habits. High losses through sweat during high-performance sports or work at high temperatures may raise requirements so that higher intakes than recommended may be needed.

During the last trimester of pregnancy the fetus retains 5 - 7.5 mg of magnesium per day. The increased requirement of pregnant women is met by the intake recommended for (young) women in combination with a usual mixed diet. During the lactation period, women provide 24 mg of magnesium in 750 ml milk which contains 32 mg of magnesium per litre on average [9]. An additional intake of 80 - 90 mg per day is needed to ensure replacement. The estimate for the recommended magnesium intake in infants is based on the magnesium supply of breast milk of 24 mg on average per day.

For the growth period, a daily retention of about 3 mg/kg has been derived from the body's magnesium content (see above). An intake of 6 mg of magnesium per kg per day as recommended in the DRI and underlying the values shown in the table should be sufficient to meet requirements [2].

Good sources are whole-grain cereal products, milk and dairy products, liver, poultry, fish, potatoes, many vegetables, soybeans, and berries, oranges and bananas. Magnesium is also supplied from coffee and tea. Food processing and preparation cause losses in magnesium which may vary considerably.

Oral intake of 3 - 5 g of magnesium compounds per day elicits diarrhoea due to osmotic processes. In cases of renal insufficiency and/or high parenteral intakes reduced functioning of the central nervous system including paresis and death have been reported. Magnesium doses of 350 mg per day in addition to the daily dietary magnesium are regarded as harmless.

References

[1] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/Main (1996), 42-45

[2] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy Press, Washington D.C. (1997), 190-249

[3] Gullestad, L., Nes, M., Ronneberg, R., Midtvedt, K., Falch, D., Kjekshsu, J.: Magnesium status in healthy free-living elderly Norwegians. J. Am. Coll. Nutr. 13 (1994), 45-50

[4] Jones, J. E., Manalo, R., Flink, E. B.: Magnesium requirements in adults. Am. J. Clin. Nutr. 20 (1967), 632-635

[5] Lakshmanan, F. L., Rao, R. B., Kim, W. W., Kelsav, J. L.: Magnesium intakes, balances, and blood levels of adults consuming self-selected diets. Am. J. Clin. Nutr. 40 (1984), 1380-1389

[6] Marxhall, D. H., Nordin, B. E., Speed, R.: Calcium, phosphorus and magnesium requirement. Proc. Nutr. Soc. 35 (1976), 163-173

[7] Milla, P. J., Aggett, P. J., Wolff, O. H., Harries, J. T.: Studies in primary hypomagnesaemia: evidence for a defective carrier-mediated small intestinal transport of magnesium. Gut. 20 (1979), 1028-1033

[8] Schwarz, R., Spencer, H., Welsh, J. J.: Magnesium absorption in human subjects from leafy vegetables, intrinsically labelled with stable ^{26}Mg. Am. J. Clin. Nutr. 39 (1984), 571-576

[9] Souci, S. W., Fachmann, W., Kraut.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

[10] Spencer, H., Fuller, H., Norris, C., Williams, D.: Effect of magnesium on the intestinal absorption of calcium in man. J. Am. Coll. Nutr. 13 (1994), 485-492

[11] Wisker, E., Nagel, R., Tanudjaja, T. K., Feldheim, W.: Calcium, magnesium, zinc, and iron balances in young women: effects of a low-phytate barley-fiber concentrate. Am. J. Clin. Nutr. 54 (1991), 553-559

Trace elements

Trace elements have been defined as inorganic food components which occur in body tissues at concentrations < 50 ppm (< 50 x 10^{-6} g/g of wet weight). Their essentiality to humans, in quantities < 50 mg/day, has been confirmed in experiments and their biochemical functions have been established.

The following trace elements will be dealt with:

Iron (Fe)

Iodine (I)

Fluoride (F)

Zinc (Zn)

Selenium (Se)

Copper (Cu)

Manganese (Mn)

Chromium (Cr)

Molybdenum (Mo)

Cobalt (Co)

Nickel (Ni)

Iron

A. Recommended intake

Age	Iron			
	mg/day		mg/MJ[1] (Nutrient density)	
	m	f[2]	m	f
Infants[3]				
0 to under 4 months[4,5]	0.5		0.3	0.3
4 to under 12 months	8		2.7	2.8
Children				
1 to under 4 years	8		1.7	1.8
4 to under 7 years	8		1.3	1.4
7 to under 10 years	10		1.3	1.4
10 to under 13 years	12	15	1.3	1.8
13 to under 15 years	12	15	1.1	1.6
Adolescents and adults				
15 to under 19 years	12	15	1.1	1.8
19 to under 25 years	10	15	0.9	1.9
25 to under 51 years	10	15	1.0	1.9
51 to under 65 years	10	10	1.1	1.4
65 years and older	10	10	1.2	1.4
Pregnant women		30		3.3
Lactating women[6]		20		1.9

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Non-menstruating women who are neither pregnant nor breast-feeding: 10 mg/day

[3] Except for premature babies

[4] Estimated value

[5] A requirement for dietary iron exists only from the 4th month due to the newborn´s reserve of placental iron (Hb iron)

[6] This applies to breast-feeding and non-breast-feeding women for replacement of iron losses during pregnancy

B. Explanations

Iron is an essential part of many oxygen- and electron-transferring systems (haemoglobin and myoglobin; different enzymes, e.g. cytochrome or ribonucleotide reductase). The human body contains an average of 2 - 4 g of iron, of which about 60% is bound to haemoglobin, 25% to ferritin and haemosiderin and about 15% to myoglobin and enzymes.

Iron deficiency may impair physical performance, interfere with thermoregulation and increase proneness to malaria. Also the immune system is dependent upon iron. Prolonged insufficient iron intake leads to iron deficiency anaemia, one of the most frequent manifestations of nutrient deficiency worldwide. Severe iron deficiency with anaemia is in the majority of cases caused by chronic blood loss due to increased menstruation or gynaecological diseases or by occult gastrointestinal blood loss. Also redistribution of iron from functional compartments to stores, e.g. in inflammation and malignant tumors, restrict iron utilization.

In Germany, the average iron intake in women is 11 mg and in men 13 mg per day [4]. Today, dietary iron deficiency is much rarer than in the past. Signs of iron deficiency anaemia have been found in about 0.6% of the population, in women twice as frequently as in men [1]. Signs of iron deficiency anaemia are especially frequent in adolescent females (causes: growth, menstruation) and in older men (causes: chronic inflammation, cancer).

During the first two years of life and during puberty, iron intake is often insufficient for the rapid growth of body mass. Hence latent iron deficiency and anaemia are most frequently diagnosed in 1- to 2-year-old children and in boys at the age of rapid pubertal growth [2, 19]. Severe iron deficiency may retard growth. Because of the cerebral iron requirement during growth adequate iron supply during childhood is of great importance [13, 20]. Especially at the age of 12 - 18 months a moderate anaemia may - probably irreversibly - affect the development of intelligence [15, 21]. Representative data of the prevalence of iron deficiency anaemia and of (the much more frequent) latent iron deficiency in children are lacking. The VERA study using serum ferritin as a diagnostic indicator of iron status showed that iron stores are depleted (ferritin < 12 µg/l) in fewer than 10% of women and in about 3% of men [14].

The requirement for iron results from intestinal, renal and dermal iron losses (about 1 mg per day). To these, losses by menstruation of about 15 mg per month must be added in women. In about 20% of women these monthly iron losses by far exceed 15 mg [8]. Growth and pregnancy increase the requirement for iron.

In most industrialized countries, according to WHO, the absorption rate of dietary iron is between 10 and 15% [6]. In iron deficient individuals it is 2 - 3 times as high. Recommendations for iron intake therefore have to specially allow for iron bioavailability; the latter may vary 10-fold, depending on the composition of the diet [9].

An intake of 15 mg of iron per day would, according to WHO, result in 1.5 - 2.2 mg of absorbed iron and thus meet the requirement of all women with normal menstruation. This assumption is supported by the fact that with an average daily iron intake of 11 mg in non-pregnant women between 15 - 44 years in the United States only 14% exhibited signs of latent iron deficiency. Women in whom menstruation is increased (e.g. by intra-uterine devices) require more iron. Postmenopausal women do not need more iron than men. This finding is supported by studies conducted in Germany [1].

Although there is no menstrual blood loss during pregnancy, requirement for iron is still increased: by about 300 mg for fetal needs, about 50 mg for placental needs and about 450 mg for the increased maternal blood volume [10]. Accordingly, a total of 30 mg of iron per day is necessary, which usually is not available in the daily diet [12].

For infants and children the daily loss of iron is estimated at 0.2 - 0.4 mg per day. For growth about 0.7 mg/day are required between the 6^{th} and 12^{th} month and 0.3 - 0.5 mg/day after the 1^{st} year of life [3, 5]. As the newborn infant has iron stores resulting from the high haemoglobin content of fetal blood and from placental sources ('placental hypertransfusion') an appreciable and increasing requirement for dietary iron does not exist before the 4^{th} month. Then about 1 mg of absorbed iron per day are required; taking the absorption rate and the variability among iron requirements into account, an intake of about 1 mg of iron per kg of body weight is recommended.

In children, about 0.8 mg of absorbed iron per day are required to replace iron losses and for growth. Higher intakes recommended for the age of puberty compensate for increased requirements of growth and in girls for menstrual losses.

A mixed diet provides 5 - 15 mg of non-haem iron and 1 - 5 mg of haem iron per day [18]. In contrast to haem iron in food of animal origin, of which more than 20% is absorbed, absorption of non-haem iron is reduced by absorption-inhibiting ligands (e.g. tannins, lignins, oxalic acids, phytates and phosphates) in staple vegetable foods (such as cereals, whole-grain rice, maize, peas, beans and lentils) [7, 11, 16]. Other inhibitors of non-haem iron absorption are wheat bran, calcium salts and milk products, soya products, black tea and coffee, also salicylates (e.g. aspirin), antacids, iron exchangers, and clofibrates. Absorption of non-haem iron is promoted only by meat, fish and poultry or by ascorbic acid

[11, 16]. Data on the effect of alcohol on iron absorption are contradictory. Persons subsisting on a haem-deficient diet (e.g. vegetarians and vegans) must concurrently eat absorption-enhancing ligands such as ascorbic or citric acid (e.g. along with fruit). Altogether, hardly more than 5% of non-haem iron supplied from food of vegetable origin is absorbed.

Because of the frequency and amount consumed and because of their iron content, bread, meat, sausages and vegetables are the most important sources of dietary iron [1].

In certain cases iron overload may occur. Excessive absorption is found in chronic alcohol abuse and in hereditary haemochromatosis [17], the latter leading to liver, pancreas and cardiac muscle damage with lethal consequences if the patient is left without medical treatment. A prooxidant action of iron has also been associated with myocardial infarction and cancer.

References

[1] Arab-Kohlmeier, L., Sichert-Oevermann, W., Schettler, G.: Eisenzufuhr und Eisenstatus der Bevölkerung in der Bundesrepublik Deutschland. Springer, Berlin, Heidelberg, New York, London, Paris, Tokyo (1989)

[2] Dallman, P. R., Siimes, M. A.: Percentile curves for hemoglobin and red cell volume in infancy and childhood. J. Pediatr. 94 (1979), 26-31

[3] Dallman, P. R.: Nutritional anemia of infancy. Iron, folic acid and vitamin B_{12}. In: Nutrition during infancy. Tsang, R. C., Nichols, B. L. (eds.), Hanley & Belfus (1988), 216-235

[4] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/Main (1996)

[5] Fairbanks, V. F., Beutler, E.: Iron. In: Modern Nutrition in Health and Disease. Shils, M. E., Young, V. R. (eds.), 7th edition, Lea & Febiger, Philadelphia (1988), 193-226

[6] FAO/WHO: Requirements of Vitamin A, Iron, Folate and Vitamin B_{12}. Report of a Joint FAO/WHO Expert Consultation. FAO Food and Nutrition Series, No. 23, FAO, Rome (1988)

[7] Hallberg, L., Bjorn-Rasmussen, E., Howard, L., Rossander, L.: Dietary heme iron absorption. A discussion of possible mechanisms for the absorption-promoting effect of meat and for the regulation of iron absorption. Scand. J. Gastroenterol. 14 (1979), 769-779

[8] Hallberg, L., Hogdahl, A. M., Nilsson, L, Rybo, G.: Menstrual blood loss - a population study. Variation at different ages and attempts to define normality. Acta Obstet. Gynecol. Scand. 45 (1966), 320-351

[9] Hallberg, L., Rossander, L.: Improvement of iron nutrition in developing countries: comparison of adding meat, soy protein, ascorbic acid, citric acid, and ferrous sulphate on iron absorption from a simple Latin American type of meal. Am. J. Clin. Nutr. 39 (1984), 577-583

[10] Hallberg, L.: Iron balance in pregnancy. In: Vitamins and Minerals in Pregnancy and Lactation. Berger, H. (ed.), Nestlé Nutrition Workshop Series, No. 16, Raven Press, New York (1988), 115-127

[11] Hallberg, L.: Iron. In: Present Knowledge in Nutrition. Olson, R. E., Broquist, H. P., Chichester, C. O., Darby, W. J., Kolbye, A. C., Stalvey, R. M. (eds.), 5th edition, Nutrition Foundation, Washington (1984), 459-478

[12] Herbert, V.: Recommended dietary intakes (RDI) of iron in humans. Am. J. Clin. Nutr. 45 (1987), 679-686

[13] International Conference on Iron Deficiency and Behavioral Development. Pollitt, E., Haas, J., Levitsky, D. A. (eds.). Am. J. Clin. Nutr. 50 Suppl. (1989), 565-705

[14] Kohlmeier, M., Thefeld, W., Stelte, W., Grimm, R., Häußler, A. et. al.: : Versorgung Erwachsener mit Mineralstoffen und Spurenelementen in der Bundesrepublik Deutschland. Differenzierung nach Alter und Geschlecht. In: Kübler, W., Anders, H. J., Heeschen, W. (eds.): VERA-Schriftenreihe Bd. V, Wiss. Fachverlag Dr. Fleck, Niederkleen (1995)

[15] Lozoff, B., Jimenez, E., Wolf, A. W.: Long-term developmental outcome of infants with iron-deficiency. N. Engl. J. Med. 325 (1991), 687-694

[16] Momsen, E. R.: Iron nutrition and absorption. Dietary factors which impact iron bioavailability. J. Am. Diet Assoc. 88 (1988), 786-790

[17] National Research Council: Iron. A report of the Subcommittee on Iron. University Park Press, Baltimore (1979)

[18] Narasinga, B. S.: Physiology of iron absorption and supplementation. Br. Med. Bull. 37 (1981), 25-30

[19] Risser, W. L., Risser, J. M. H.: Iron-deficiency in adolescents and young adults. Phys. Sportsmed. 18 (1990), 87-101

[20] Walter, T., Kovalskys, J., Stekel, A.: Effect of mild iron deficiency on infant mental development scores. J. Pediatr. 102 (1983), 519-522

[21] Walter, T.: Impact of iron deficiency on cognition in infancy and childhood. Eur. J. Clin. Nutr. 47 (1993), 307-316

Iodine

A. Recommended intake

Age	Iodine Germany Austria			Iodine WHO Switzerland		
	µg/day	µg/MJ[1] (Nutrient density)		µg/day	µg/MJ[1] (Nutrient density)	
		m	f		m	f
Infants						
0 to under 4 months[2]	40	20	21	50	25	26
4 to under 12 months	80	27	28	50	17	17
Children						
1 to under 4 years	100	21	23	90	19	20
4 to under 7 years	120	19	21	90	14	16
7 to under 10 years	140	18	20	120	15	17
10 to under 13 years	180	19	21	120	13	14
13 to under 15 years	200	18	21	150	13	16
Adolescents and adults						
15 to under 19 years	200	19	24	150	14	18
19 to under 25 years	200	19	25	150	14	19
25 to under 51 years	200	20	26	150	15	19
51 to under 65 years	180	20	24	150	16	20
65 years and older	180	22	26	150	18	22
Pregnant women	230		25	200		22
Lactating women	260		24	200		19

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Estimated value

B. Explanations

Dietary iodine and iodate are rapidly and nearly completely absorbed, the latter after reduction to iodide. Given a continuous intake of 200 µg iodine/day about 15% is taken up by the thyroid gland within 24 hours. With lower iodine intakes or an iodine depleted thyroid gland more iodine is absorbed due to an active autoregulatory mechanism.

Iodine acts as part of the thyroid hormones. It is linked to the body's selenium status through selenium containing iodine-thyronine deiodinases. The latter activate both conversion of the prohormone thyroxine (T_4) to the active thyroid hormone T_3 and degradation of these hormonal compounds. The iodine content of an adult has been estimated at 10 - 20 mg. 8 - 15 mg of these are found in the thyroid gland. Iodine is mainly excreted through the kidneys after the thyroid hormones are partly deiodized. 15 - 20 µg of iodine per day are excreted in the faeces [1]. Urinary iodine excretion is frequently taken as a practicable measure to assess a person's iodine status.

According to a definition by WHO, Germany is among the world's iodine-deficient areas. These populations are at risk of iodine deficiency disorders, mainly endemic goitre and endemic cretinism [7]. Goitre can also arise from causes other than iodine deficiency, among them goitrogenic substances (e.g. glucosinolates as goitrogens in cabbage, but also isothiocyanates, thiocyanates or nitrates) [15].

The synthesis of thyroid hormone is the main parameter for deriving iodine requirement. Variables to be considered are the re-utilization of iodine shown in balance studies, the connection between iodine status and goitre frequency in epidemiological studies, the relation between long-term iodine intake and iodine content of the thyroid gland, and inactivation of active autonomous thyroid adaptation mechanisms once a certain level of iodine intake has been exceeded. To allow for these criteria, urinary iodine excretion in adults should not be less than 100 µg/day. A median urinary iodine excretion of 108 µg/day for young men was found in an iodine monitoring campaign in 1996 [11]. To ensure an adequate iodine status, iodine excretion in the faeces (15 - 20 µg/day) must be compensated for. It should also be considered that the iodine content of food varies greatly depending on the region and season, that, furthermore, food preparation may involve iodine losses and that a relatively low selenium intake could reduce the amount of T_3 converted from T_4 (thyroxine).

WHO proposes an intake of 2 µg iodine/kg of body weight per day [17]. For correction of prolonged iodine deficiency, however, higher intakes are needed to replenish the thyroid gland with iodine.

The influence of goitrogenic compounds should be considered as well. The risk of endemic goitre increases with increasing content of goitrogens in food and drinking water. In school children a dose-effect relationship between nitrate load and frequency of goitre has been shown [8]. The risk can be diminished by increased iodine intake, as a competitive iodine antagonism exists for some of the goitrogens.

Lasting iodine deficiency in Germany and the above mentioned influences were reason to retain a recommended intake of 200 µg iodine/day as recommended

up to now and not to follow WHO who proposed 150 µg/day in 1996. In Switzerland, an iodized salt programme practised over decades has resulted in better supply than in Germany and Austria and the WHO recommendations were adopted.

Fetal iodine supply, iodine concentration in breast milk and iodine intake in an exclusively breast-fed infant depend on the mother's iodine status [16]. During pregnancy iodine requirement is increased due to an increased renal blood flow and concomitant increased urinary iodine excretion. Pregnant women therefore should make sure that they obtain sufficient iodine; adequate daily intakes in pregnant women are 230 µg in Germany and Austria and 200 µg in Switzerland.

During the lactation period, iodine excreted in breast milk has to be replaced. For breast-feeding women, the recommended iodine intake is increased to 260 µg/day and 200 µg/day, respectively. Commercial infant formulae provide adequate iodine quantities because of added sodium- and potassium-iodide. In regions where iodine supply is critical, manifestations of goitre mainly affect pregnant and lactating women but also the newborn and adolescents at the age of puberty [7, 12].

The iodine content of food of vegetable and animal origin largely depends on the iodine content of soils and the iodine supply of agricultural livestock leading to a great variability among iodine contents. Saltwater fish and other seafood usually are rich in iodine; so are milk and eggs provided the animals were adequately fed. Part of the iodine is lost during cooking. This also applies to iodine in iodized table salt.

Iodized salt commercially available in Germany, a mixture of table salt and iodate, contains iodine in quantities of at least 15 mg to a maximum of 25 mg/kg table salt. It is legally registered for use in private households and catering institutions and for industrial production of food intended for general consumption. Meat and sausages may be produced using iodized nitrite salts (iodine content also 15 - 25 mg/kg). So-called 'Reformsalz' and 'sea salts', if non-iodized, only contain insufficient iodine quantities. In individuals subsisting on an imbalanced vegetarian or low-salt diet and in those with cow's milk allergy, lactose intolerance or fish allergy iodine supplementation in tablet form may be indicated upon medical advice [5, 6, 9].

In Austria the iodine content of table salt was raised to 20 mg/kg by potassium iodide in 1990. Although this enhanced the population's iodine supply, low urinary iodine excretion is still relatively common in children and adolescents [4].

Switzerland has consequently implemented their national iodized salt programme (iodine content of 20 - 30 mg/kg table salt); as a result, the incidence of goitre is very low.

Iodine-induced goitre, genuine thyrotoxic crisis or iodide acne do not occur after physiological quantities of dietary iodine or iodine from iodized table salt. Complications of this kind have only been observed when the recommended intake was exceeded by several orders of magnitude [13]. For the development of iodine-induced goitre, a *chronically* increased iodine intake in unphysiological quantities (e.g. iodine-containing medications, disinfectants) is a requirement. The same applies to the development of hyperthyroidism in a concurrent autonomous thyroid gland. Contrast media with prolonged retention time (e.g. oral contrast media for use in cholecystographies) may, in cases of a concurrent autonomous thyroid gland, induce hyperthyroidism.

The tolerable upper intake level according to WHO is 1 mg/day. In Germany as well as in other countries [3, 14], however, unrecognized functional autonomia of the thyroid gland must be expected, especially in older individuals following prolonged iodine deficiency. Under these conditions dietary iodine intake in adults should not exceed 500 µg/day in general. This dose is incapable of inducing acute severe hyperthyroidism in cases with concurrent compensated autonomia of the thyroid gland. However, it is still capable of inducing hyperthyroidism, depending on the progression of the autonomia and on the iodine dose [10]. These hyperthyroidisms become accessible to early therapy. Incidence of such hyperthyroidism will clearly decrease with enhanced iodine supply of the population [2]. Also Basedow hyperthyroid cases receiving medical treatment may use iodized table salt and eat food containing iodized salt.

References

[1] Anke, M., Glei, M., Groppel, B., Rother, C., Gonzales, D.: Mengen-, Spuren- und Ultraspurenelemente in der Nahrungskette. Nova Acta Leopoldina NF 79, Nr. 309 (1998), 157-190

[2] Baltisberger, B. L., Minder, C. E., Bürgi, H.: Decrease of incidence of toxic nodular goitre in a region of Switzerland after full correction of mild iodine deficiency. Eur. J. Endocrinol. 132 (1995), 546-549

[3] Bürgi, H., Baumgartner, H., Steiger, G.: Gibt es eine obere Verträglichkeitsgrenze der alimentären Jodzufuhr? Schweiz. Med. Wochenschr. 112 (1982), 2-7

[4] Elmadfa, I., Koenig, J. S.: Iodine status of Austrian children and adolescents. In: Sandström, B., Walter, P. (eds.): Role of Trace Elements for Health Promotion and Disease Prevention. Bibl. Nutr. Dieta Basel Karger No. 54 (1998), 58-66

[5] Großklaus, R., Somogyi, A.: Notwendigkeit der Jodsalzprophylaxe. bga-Schriften, MMV Medizin-Verlag, München (1994)

[6] Großklaus, R.: Ernährungsrisiko durch Jodmangel und Strategien der Beseitigung. In: Somogyi, D.; Großklaus, D. (eds.): Gesundheit und Umwelt 92. bga-Schriften 7/92

[7] Gutekunst, R., Smolarek, H., Wächter, W., Scriba, P. C.: Strumaepidemiologie IV Schilddrüsenvolumina bei deutschen und schwedischen Schulkindern. Dtsch. Med. Wochenschr. 110 (1985), 50-54

[8] Höring, H., Nagel, M., Haerting, J.: Das nitratbedingte Strumarisiko in einem Endemiegebiet. Medizinische Informatik und Statistik 72 (1991), 147-153

[9] Hötzel, D., Scriba, P. C., Meinhart, E.: Deckung des Jodbedarfs. In: Spurenelemente und Ernährung. Wolfram, G., Kirchgeßner, M. (eds.), Wissenschaftliche Verlagsgesellschaft, Stuttgart (1990), 83-99

[10] Livadas, D. P., Koutras, D. A., Souvatzoglou, A., Beckers, C.: The toxic effects of small iodine supplements in patients with autonomous thyroid nodules. Clin. Endocrinol. 7 (1977), 121-127

[11] Manz, F. et al.: Jod-Monitoring 1996. Schriftenreihe des Bundesministeriums für Gesundheit; Band 110. Nomos-Verlagsgesellschaft, Baden-Baden (1998)

[12] Manz, F.: Jodmangel - Jodbedarf - Jodmangelprophylaxe - Jodexzeß bei Kindern. Der Kinderarzt 26 (1995), 1594-1598

[13] Pennington, J. A.: A review of iodine toxicity reports. J. Am. Diet. Assoc. 90 (1990), 1571-1581

[14] Phillips, D. I., Nelson, M., Barker, D. J., Morris, J. A., Wood, T. J.: Iodine in milk and the incidence of thyrotoxicosis in England. Clin. Endocrinol. 28 (1988), 61-66

[15] Pickardt, R. C., Köbberling, J. (eds.): Struma. Springer, Berlin-Heidelberg-New York (1990)

[16] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

[17] WHO/UNICEF/ICCIDD: Recommended Iodine levels in Salt and Guidelines for Monitoring their Adequacy and effectiveness WHO/NUT/96.13 (1996)

Fluoride

A. Guiding values for total intake of fluoride (diet, drinking water and supplements) and fluoride supplementation for dental caries prevention

Age	Adequate total intake of fluoride (mg/day)[1,2,3]		Recommended supplements taking into account the fluoride concentration of drinking water, and the use of fluoridated table salt (250 mg/kg)[4,5]				
			Fluoride in drinking water (mg/l)				
			< 0.3		0.3-0.7		> 0.7[6]
	m	f	Fluoridated table salt[7]	Tablets (mg)	Fluoridated table salt	Tablets (mg)	–
Infants							
0 to under 4 months	0.25		Tabl. 0.25	0.25	+	0	–
4 to under 12 months	0.5		Tabl. 0.25	0.25	+	0	–
Children							
1 to under 4 years	0.7		Tabl. 0.25	0.25	+	0	–
4 to under 7 years	1.1		+	0.5	+	0.25	–
7 to under 10 years	1.1		+	1.0	+	0.5	–
10 to under 13 years	2.0		+	1.0	+	0.5	–
13 to under 15 years	3.2	2.9	+	1.0	+	0.5	–
Adolescents and adults							
15 to under 19 years	3.2	2.9	+	1.0	+	0.5	–
19 to under 25 years	3.8	3.1	+	1.0	+	0.5	–
25 to under 51 years	3.8	3.1	+	1.0	+	0.5	–
51 to under 65 years	3.8	3.1	+	1.0	+	0.5	–
65 years and older	3.8	3.1	+	1.0	+	0.5	–
Pregnant women		3.1	+	1.0	+	0.5	–
Lactating women		3.1	+	1.0	+	0.5	–

[1] The risk of fluoride accumulation (chronic overdosage) is very small because of the high growth rate during the 1st half year of life. Because of delayed mineralization, fluorosis of the permanent teeth by fluoride supplements during the first 6 months of life is neither to be expected nor has it been observed.

[2] Fluoride intake from solid food, drinking water, beverages and food supplements. In prolonged intake of doses exceeding the upper limit (about 0.1 mg/kg/day), especially during the age period of 2 to 8 years, enamel mottling ('dental fluorosis') may occur.

[3] Corresponding to about 0.05 mg/kg body weight in infants and children.

[4] Standard situation: fluoride in drinking water < 0.3 mg/kg, table salt not fluoridated, no special diet. A brief fluoride history should be taken before fluoride tablets are prescribed.

[5] Balanced diets, e.g. for treatment of metabolic disorders, are usually fortified. Then additional fluoride intake is not recommended. Attention should be paid to the information provided by manufactures.

[6] Fluoride content of drinking water (mg/l). If the water contains more than 0.7 mg/l, neither fluoride tablets nor fluoridated table salt are recommended.

[7] In Germany fluoridated table salt contains 250 mg of fluoride per kg of table salt. Intake of fluoride from table salt in infants and young children is so low that additional fluoride tablets seem to be justified for these age groups even if fluoridated table salt is used by the family (+).

B. Explanations

Fluoride is a normal constituent of the human body. Its concentration in bones and teeth of about 200 - 2000 mg/kg is about 10,000 times that prevailing in body fluids and soft tissues [1, 2, 3]. Because of its proven dental caries preventing action, for which evidence has been found in many studies, fluoride has been classified with those elements which are indispensable for human health [2, 5]. There are indications that fluoride is involved in the mineralization of bones and teeth [4, 11, 13]. Beneficial effects of low-dose fluoride supplements on growth and dental eruption have been reported suggesting a general biological importance of fluoride [2].

Dental caries is caused by many factors. Fluoride, if ingested in adequate quantities, is beneficial for dental health in both the pre- and posteruptive phase of dental development in that it enhances resistance to acid attacks by cariogenic oral bacteria and intensifies remineralization of initial lesions.

For optimal dental health, fluoride intakes, on the one hand, must be sufficiently high. On the other hand chronic excessive fluoride intake may cause enamel mottling (dental fluorosis). Mild to moderate dental fluorosis is usually associated with very low caries attacks and has no adverse effects on health. In regions where the drinking water is fluoridated, minor dental fluorosis in up to 10% of the population is regarded as harmless [5].

Water-soluble fluoride, e.g. sodium fluoride (NaF) is nearly completely absorbed. The bioavailability of fluoride may be substantially reduced in the presence of calcium, magnesium, aluminium, iron or other cations. Absorbed fluoride is rapidly bound to the minerals in bones and teeth. Most of the non-retained or metabolic fluoride is excreted through the kidneys. In balance studies infants and small children retain 50 - 90% of soluble fluoride, adults only 10% or less. The remaining fluoride is excreted through the kidneys and to a small extent also into the intestine [1, 2].

Fluoride intake from the majority of foods is low. Children ingest 0.1 - 0.2 mg/day, adults 0.4 - 0.6 mg/day. This applies to the majority of regions in Germany where the fluoride content of drinking water is less than 0.3 mg/l [1, 2, 3].

Guiding values for adequate total intake of fluoride have been based on observations in regions with temperate climate where the fluoride concentration of drinking water is about 1 mg/l and provides optimal protection against dental caries [7]. There, the average daily intake in children is 0.05 mg of fluoride per kg of body weight [5]. This quotient has also been taken as the basis for the guiding values for adults.

Low natural fluoride concentrations in drinking water have prompted many countries to slightly raise the fluoride level (fluoridation of drinking water). In Germany, legal food regulations do not permit a general fluoridation of drinking water. Other measures of fluoride prophylaxis have therefore been taken. According to surveys, about 80% of infants and 40 - 60% of small and school children regularly take fluoride tablets. In 1992 fluoridated table salt was commercially introduced; its market share has ever since been continuously growing [1, 10]. These developments have been the reason to modify the practical guidelines for use of fluoride supplements or fluoridated table salt [12]. Accordingly, private households should only employ one form of systematic fluoride prophylaxis, i.e. either by fluoridated table salt or fluoride tablets. Excepted from this rule are infants and small children because they only ingest very small quantities of salt. They should take fluoride tablets, even if fluoridated salt is used in their households [1, 12].

Fluoride supplements and fluoridated table salt are not required in regions with naturally high fluoride concentrations (> 0.7 mg/l) in the drinking water. Information about fluoride concentrations in regional drinking water may be obtained from public health departments. If mineral water with a naturally high fluoride content is continuously used in a household it should be considered as high-fluoride drinking water [12].

In Germany fluoridated table salt contains 250 mg fluoride/kg [1, 10]. Health problems following excessive intake are unlikely to occur even when a diet including fluoridated table salt is supplemented with fluoride tablets at the recommended dose [1]. Health problems may arise, however, when, in addition, toothpaste for adults which usually contains 1000 to 1500 mg of fluoride/kg is used to brush the teeth of infants and school children and when the children swallow major parts of the toothpaste [9].

Fluoride supplements have systemic and topical effects. In school children, adolescents and adults the topical use of fluoride in the form of tooth paste and professional dental applications (in addition to systemic prophylaxis, e.g. by fluoridated table salt) seems to be reasonable because their teeth are completely developed or erupted. During the first three years of life, however, fluoride-free toothpaste should be used. If the practice of topical fluoride administration is also extended to small children or even infants one should be aware of the risk that major parts of the toothpaste are swallowed, leading to fluoride overdosage [9] or even acute toxicity. Toothpaste for children under 6 years must have a low fluoride concentration (250 to 500 mg/kg) and be dosed in the smallest portions. Dental care using fluoride toothpaste in infants and small children would practically equal systemic fluoride administration; any other form of systemic prophylaxis, i.e. by fluoridated table salt or tablets, would then have to be stopped.

Infants and children fed balanced formula diets need no systemic fluoride prophylaxis because, in compliance with EU regulations, balanced diets are adequately fortified with all trace elements including fluoride [8]. If, in exceptional cases, diets are not fortified manufacturers have to explicitly point out this fact. Those who are responsible for children fed special formula diets should take notice of this point.

It is inadvisable to give fluoride supplements to premature and small-for-date infants as long as they do not weigh at least 3000 g and continue to grow well.

Fluoride may have acute toxic effects if more than 1 mg of fluoride per kg of body weight are ingested at once [5, 6]. First manifestations are nausea, vomiting and abdominal pain. Chronic fluoride intakes only a little in excess of the recommended doses, e.g. twice the guiding value for intake during the first 8 years of life, elicit small symmetric, mostly band-shaped white opacities on the dental enamel. Higher chronic overdoses may lead to brown staining of the teeth. Hence, in children up to 8 years of age, maximum intakes should not exceed 0.1 mg/kg of body weight. Beyond the age of 8 years dental fluorosis as a consequence of chronic fluoride overdosage is irrelevant because by then enamel development is largely completed.

Daily fluoride intakes of 10 mg or more over a period of 10 years at least are needed to affect the skeletal system. If the exposure in a region is still higher (20 - 80 mg/person/day for 10 years or more) moderate to severe skeletal fluorosis is found; manifestations involve arthralgia and ankylosis due to ossification of tendons and joint capsules [5].

References

[1] Bergmann, K. E., Bergmann, R. L.: Salt fluoridation and general health. Adv. Dent. Res. 9 (2) (1995), 138-143

[2] Bergmann, R. L., Bergmann, K. E.: Fluoride Nutrition in Infancy - Is there a Biological Role of Fluoride for Growth? In: Chandra, R. K. (ed.): Trace Elements in Nutrition of Children II. Nestlé Nutrition Workshop Series, Vol. 23, Raven Press, New York (1991), 105-117

[3] Bergmann, R. L., Bergmann, K. E.: Die Fluoridversorgung des Menschen. In: G. Wolfram, M. Kirchgeßner (Hrsg.): Spurenelemente und Ernährung. Wissenschaftl. Schriftenreihe der Ernährungsgesellschaften Deutschland, Österreich, Schweiz. Wissenschaftliche Verlagsgesellschaft, Stuttgart (1990), 47-66

[4] Farley, J. R., Wergedal, J. E., Baylink, D. J.: Fluoride directly stimulates proliferation and alkaline phosphatase activity of bone-forming cells. Science 222 (1983), 330-332

[5] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy Press, Washington D.C. (1997), 288-313

[6] Gessner, B. D., Beller, M., Middaugh, J. P., Whitford, G. M.: Acute fluoride poisoning from a public water system. N. Engl. J. Med. 330 (1994), 95-99

[7] Horowitz, H. S.: The effectiveness of community water fluoridation in the United States. J. Public Health Dent. 56 (1996), 253-258

[8] Kersting, M., Chahda, Ch., Schöch, G.: Fluoridzufuhr bei Säuglingen mit bilanzierten Diäten. Ernährungs-Umschau 46 (1999), 12-13

[9] Kumar, J. V., Swango, P. A., Lininger, L. L., Leske, G. S., Green, E. L., Haley, V. B.: Changes in dental fluorosis and dental caries in Newburgh and Kingston, New York. Am. J. Public Health 88 (1998), 1866-1870

[10] Marthaler, T. M., Martin, A.: Aktueller Stand der Salzfluoridierung. 3. Teil: Überwachung der Fluoridversorgung ganzer Bevölkerungen. Oralprophylaxe 8 (1986), 154-163

[11] Newesely, H.: Changes in crystal types of low solubility calcium phosphates in the presence of accompanying ions. Arch. Oral Biol. 6 Special Suppl. (1961), 174-180

[12] Schmidt, E., Wolfram, G., Schmalz, G.: Empfehlungen zur Kariesprävention mit Fluoriden (DGZMK/DGKJ/DGE). Dtsch. Zahnärztl. Zeitschr. 51 (1996), 725-726

[13] Varughese, K., Moreno, E. C.: Crystal growth of calcium apatites in dilute solutions containing fluoride. Calcif. Tissue Int. 33 (1981), 431-439

Zinc

A. Recommended intake

Age	Zinc			
	mg/day		mg/MJ[1] (Nutrient density)	
	m	f	m	f
Infants				
0 to under 4 months[2]	1.0		0.5	0.5
4 to under 12 months	2.0		0.7	0.7
Children				
1 to under 4 years	3.0		0.6	0.7
4 to under 7 years	5.0		0.8	0.9
7 to under 10 years	7.0		0.9	1.0
10 to under 13 years	9.0	7.0	1.0	0.8
13 to under 15 years	9.5	7.0	0.8	0.7
Adolescents and adults				
15 to under 19 years	10.0	7.0	0.9	0.8
19 to under 25 years	10.0	7.0	0.9	0.9
25 to under 51 years	10.0	7.0	1.0	0.9
51 to under 65 years	10.0	7.0	1.1	0.9
65 years and older	10.0	7.0	1.2	1.0
Pregnant women				
from the 4th month		10.0		1.1
Lactating women		11.0		1.0

[1] Calculated for adolescents and adults with predominantly sedentary activity (PAL 1.4)

[2] Estimated value

B. Explanations

Humans contain about 2 g of zinc, with greatly varying levels in individual organs and tissues. About 70% is located in bones, skin and hair. Zinc is slowly metabolized in tissues. There are no large zinc stores in the body which could be mobilized at times of shortage. Regular zinc intake is therefore essential.

Zinc has specific metabolic functions such as constituent or activator of many enzymes of the protein-, carbohydrate-, fat- and nucleic acid metabolism, of hormones and receptors as well as of insulin storage and in the immune system.

Severe zinc deficiency leads to reduced taste sensation, poor appetite, dermatitis, alopecia, diarrhoea and neuropsychic disorders. Retarded growth, disturbed male sexual development and reproductive functions, delayed wound healing and increased proneness to infections as manifestations of an impaired immune system have all been reported [1, 2]. Acrodermatitis enteropathica is an autosomal-recessively transmitted disorder caused by reduced dietary zinc absorption.

Zinc deficiency occurs in malabsorption syndromes, with total parenteral nutrition, treatment with chelating agents and extensive burns. Infants are at higher risk for zinc deficiency towards the end of the period of rapid growth.

Net absorption of zinc has a considerable enteropancreatic circulation of zinc superimposed. For meeting zinc requirement, however, utilization of dietary zinc is of essential importance [9, 10]. The latter mainly depends on the net requirement, the level of intake and zinc status, but also on the chemical bonds of zinc, interactions with other dietary components, and other conditions. Zinc absorption from food of animal origin is generally better than that from vegetable foods. The bioavailability of zinc from cow's milk is much lower than from human milk. This is due to absorption-promoting ligands (peptides, amino acids and citrate) in human milk and absorption-inhibiting factors in cow's milk (casein, calcium). The complexing agents histidine and cysteine enhance absorption while phytic acid, which binds zinc, inhibits absorption. To release zinc from the phytic complex a microbial phytase is needed which is not synthesized in the human body. Vegetarians, due to the higher intake of dry mass, ingest one third more zinc than persons on a mixed diet [8], but zinc bioavailability from a vegetarian diet is lower. A high-calcium diet also reduces zinc absorption. Zinc utilization is also influenced by stress, surgical treatment, parasitic diseases and infections. The average absorption rate for zinc from a mixed diet today is estimated at about 30% [7, 13].

Zinc requirements are derived from zinc balance studies and from the replacement of obligatory zinc losses [1, 4, 7]. The obligatory excretory and dermal loss of zinc has been found to be 2.2 mg/day in men and 1.6 mg/day in women [4]. Given an average absorption rate of 30%, requirement for zinc replacement in men is about 7.5 mg/day and in women 5.5 mg/day. Adding an allowance of 30% corresponding to a coefficient of variation of 15% one arrives at a recommended intake of 10 mg/day for men and of 7.0 mg/day for women. These values, owing to most recent insights into absorption rate and obligatory loss of zinc, are lower than those provided in the 5th revised edition (1991) of

Empfehlungen für die Nährstoffzufuhr (Recommendations on Nutrient Intake) of the DGE.

Exclusively breast-fed infants receiving an average of 1.0 mg of zinc per day [12] in 750 ml of breast milk are adequately supplied. Four months post partum the zinc concentration in breast milk is about 1.2 mg/l [11]. Zinc intake increases when the infant is fed supplementary food [6]. In children and adolescents, recommended intakes have gradually been adapted to age to ensure a largely constant nutrient density.

The average daily extra requirement for absorbed zinc has been estimated at 0.8 mg for the second half of pregnancy and at 1.0 mg for the period of lactation. Although adaptation mechanisms assumed to ensure better zinc absorption during pregnancy have been a matter of recent debate and although zinc supplementation yielded no advantages [5], increased intakes of 3 mg/day starting in the second trimester and of 4 mg/day during the lactation period seem advisable.

Good sources of zinc are beef, pork, poultry, eggs, milk, and cheese. High-zinc food (e.g. whole wheat grain) may sustain great losses during food processing and preparation (e.g. flour, depending on the extraction rate achieved by milling). However, zinc concentrations may also increase by cooking or during storage of acid-containing food or in water in electro-galvanized containers.

The threshold of zinc toxicity is very high. Zinc intoxication may follow intake of acid-containing food or water from galvanized containers. Acute intoxication by e.g. 2 g of zinc causes gastrointestinal disorders and fever; chronic intoxication with > 110 mg per day leads to hypochromic anaemia and neutropenia, probably due to interaction with copper [3]. Even short-term intakes of about 50 mg of zinc per day interfere with iron and copper metabolism [14]. Zinc intakes of more than 30 mg/day are therefore advised against.

References

[1] Commission of the European Communities: Reports of the Scientific Committee for Food. Nutrient and energy intakes for the European Community. Thirty-first series. Zinc. Office for Official Publications of the European Communities, Luxemburg (1993)

[2] Gibson, R. S., Vanderkooy, P. D., MacDonald, A. C., Goldman, A., Ryan, B. A., Berry, M.: A growth limiting, mild zinc-deficiency syndrome in some southern Ontario boys with low height percentiles. Am. J. Clin. Nutr. 49 (1989), 1266-1273

[3] Gyorffy, E. J., Chan, H.: Copper deficiency and microcytic anemia resulting from prolonged ingestion of over the counter zinc. Am. J. Gastroenterol. 87 (1992), 1054-1055

[4] King, J. C., Turnlund, J. R.: Human zinc requirements. In: Mills, C. F. (ed.): Zinc in Human Biology. Springer Verlag, London (1989), 335-350

[5] Mahomed, K., James, D. K., Golding, J., McCabe, R.: Zinc supplementation during pregnancy: a double blind randomised controlled trial. BMJ 299 (1989), 826-830

[6] Michaelsen, K. F., Samuelson, G., Graham, T. W., Lönnerdal, B.: Zinc intake, zinc status and growth in a longitudinal study of healthy Danish infants. Acta Paediatr. 83 (1994), 1115-1121

[7] Milne, D. B., Canfield, W. K., Mahalko, J. R., Sandstead, H. H.: Effect of dietary zinc on whole body surface loss of zinc: impact on estimation of zinc retention by balance method. Am. J. Clin. Nutr. 38 (1983), 181-186

[8] Röhrig, B., Anke, M., Drobner, C., Jaritz, M., Holzinger, S.: Zinc intake of German adults with mixed and vegetarian diets. Trace Elements and Electrolytes. Vol. 15, (1998), 81-86

[9] Sandström, B., Arvidsson, B., Cederblad, A., Björn-Rasmussen, E.: Zinc absorption from composite meals. I. The significance of wheat extraction rate, zinc, calcium and protein content in meals based on bread. Am. J. Clin. Nutr. 33 (1980), 739-745

[10] Sandström, B., Cederblad, A.: Zinc absorption from composite meals. II. Influence of the main protein source. Am. J. Clin. Nutr. 33 (1980), 1778-1783

[11] Sievers, E., Oldigs, H. D., Dorner, K., Schaub, J.: Longitudinal zinc balances in breast-fed and formula-fed infants. Acta Paediatr. 81 (1992), 1-6

[12] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwerttabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)

[13] Taylor, C. M., Bacon, J. R., Aggett, P. J., Bremner, I.: Homeostatic regulation of zinc absorption and endogenous losses in zinc-deprived men. Am. J. Clin. Nutr. 53 (1991), 755-763

[14] Yadrick, H. K., Kenney, M. A., Winterfeld, E. A.: Iron, copper and zinc status: response to supplementation with zinc or zinc and iron in adult females. Am. J. Clin. Nutr. 49 (1989), 145-150

Selenium

A. Estimated values for adequate intake

Age	Selenium µg/day
Infants	
0 to under 4 months	5-15
4 to under 12 months	7-30
Children	
1 to under 4 years	10-40
4 to under 7 years	15-45
7 to under 10 years	20-50
10 to under 13 years	25-60
13 to under 15 years	25-60
Adolescents and adults	
15 to under 19 years	30-70
19 to under 25 years	30-70
25 to under 51 years	30-70
51 to under 65 years	30-70
65 years and older	30-70
Pregnant women	30-70
Lactating women	30-70

B. Explanations

Selenium has essential functions as part of glutathione-peroxidases, deiodases, thioredoxin reductase, plasma selenoprotein P and of some other selenocysteine-containing proteins of the reproductive organs [15, 18]. The four glutathione peroxidases known so far degrade hydrogen peroxide, low-molecular hydroperoxides and phospholipid hydroperoxides. Iodine thyronine deiodases are essential for activation and conversion of the prohormone thyroxine (T_4) to the active thyroid hormone triiodothyronine T_3; they also contribute to the degradation of thyroxine and T_3 [8]. The enzymatic function of thioredoxin reductase is linked to the presence of selenocysteine. Thioredoxin reductase mediates - either directly or via thioredoxin - the reduction of protein disulfide bridges of several other biomolecules and primarily of transcription factors. It thus influences processes of cellular proliferation and differentiation. Selenoprotein P and

other selenoproteins are assumed to have antioxidant action [2]. Epidemiological studies indicate direct anticarcinogenic and protective effects of selenium. Furthermore, they have provided evidence for immunomodulatory effects of selenium or selenoproteins. Protection of lipids against oxidation involves a synergistic relationship between selenium and tocopherols [3].

A relationship has been reported between inadequate selenium intake and Keshan disease, a cardiomyopathy; deficiency symptoms appear when selenium intakes fall below 10 µg per day [4]. Selenium deficiency has also been observed in patients on long-term total parenteral nutrition not supplemented with selenium. Signs of deficiency included muscular dysfunction. Selenium intakes may also be inadequate in newborn infants on total parenteral nutrition, with special diets (e.g. PKU diet) [10] and absorption disorders (mucoviscidosis, short gut syndrome, etc.). Kashin-Beck disease, an osteoarthropathy, has been attributed to low selenium intake, but iodine deficiency or mycotoxins are also discussed.

In patients on chronic dialysis very low plasma selenium concentrations and plasma glutathione peroxidase activities are frequently measured; after a long time, values may be as low as those prevailing in regions deficient in selenium. Here selenium supplementation may be indicated. Whether this equally applies to persons at risk for higher selenium losses (patients suffering from trauma, severe burns, blood losses, and with increased selenium excretion in urine and faeces) remains to be clarified.

Further risk groups for inadequate selenium intake are individuals on unbalanced diets, e.g. strict vegans, and on low-energy and low-protein diets [12].

So far, recommendations for selenium intake, including estimated safety factors, were derived from plasma glutathione peroxidase activity after selenium supplementation in selenium deficiency diseases. In the meantime, however, other essential selenocysteine-containing proteins have been discovered; thus, diagnostic endpoints of adequate or optimal selenium status are still a matter of scientific debate [9]. There is a varying dependence of different glutathione peroxidase activities on the availability of selenium so that maximum activities are achieved at different selenium concentrations. Furthermore, increases in plasma selenoprotein activity as a result of selenium supplementation depend on the chemical selenium compound used (sodium selenite, selenomethionine containing yeast or other organic selenium compounds) [1].

In 1989 the recommendation (RDA) by the National Research Council of the USA (0.87 µg/kg body weight = 70 µg for men and 55 µg for women) was based on saturation of the classical glutathione peroxidase. In 1996 WHO recommended selenium intakes (based on two-thirds saturation of glutathione

peroxidase activity) of 30 µg/day for women and of 40 µg/day for men [20]. These values do not yet account for the preferential saturation of deiodases and selenoprotein P discovered recently. A recent study in New Zealand which allowed for two-thirds saturation of glutathione peroxidase, deiodases and selenoprotein P arrived at a lower estimate of 39 µg of selenium per day which the authors consider to be a realistic reference value [7].

In 1989 the daily dietary selenium intake in West German adults was 47 µg for men and 38 µg for women [11]. More recent duplicate studies arrived at average intakes in German adults of 41 µg/day for men and 30 µg/day for women [6]; in adult Austrians intakes averaged 35.5 µg/day [14]. These levels largely correspond to those obtained in duplicate studies in neighbouring countries (Belgium 31 µg, Sweden 40 µg and France 48 µg/day) [6, 13, 16]. Given dietary habits common to these countries unequivocal signs of selenium deficiency have not been reported. In Germans on a typical diet plasma selenium concentrations are in the normal range (> 50 µg/l) [3]. More recent data from Switzerland indicate a better selenium status than in Germany due to high-selenium cereals imported from the USA. Serum selenium concentrations in the Swiss were between 64 and 102 µg/l [22]. The data in Europe and the present state of knowledge suggest that 30 - 70 µg of selenium per day ensure an adequate intake. As actual intakes are close to the lower limit of this range and as selenium has been found to enhance antioxidative capacity (see section II, page 194) selenium supply among Europeans should be kept under careful observation.

Dietary selenium supplementation has so far not been sufficiently substantiated nor does it seem necessary at present. Utilization of dietary supplements in the body depends on the kind of selenium compound ingested and on the composition of the diet. Selenomethionine, even if taken in small doses, has been found to lead to selenium storage after saturation of glutathione peroxidase. Whether these stores are harmless or not remains to be shown (e.g. storage of selenium-heavy metal complexes in internal organs, transfer to fetus and infant). Another argument which speaks for a restriction to natural dietary selenium intake is provided by the fact that Germany is not yet among the regions with adequate iodine supply. An isolated increase in selenium intake could activate deiodases, so that more thyroxine would be converted to triiodothyronine. Consequently, hypothyroidism might be induced by inhibition of TSH release [19].

Selenium is mainly supplied from meat, fish and hen's eggs. Good sources are also lentils and asparagus. In Germany, little selenium from the average soil is available to plants; so vegetable protein, cereals and bread contribute only insignificantly to dietary selenium supply, in contrast to USA and Canada where soils contain more selenium. Potential losses of the highly volatile selenium during food processing as well as imbalanced diets should therefore be avoided.

Data on selenium content in breast milk vary greatly [17]. This is due to considerable regional differences and partly also to the failure to notice a substantial decrease in the selenium concentration of breast milk in the early lactation period. During the first months of life, low selenium intake is sufficient as selenium has been stored in the liver before birth. Dietary selenium levels increase once the infant is fed supplementary food.

Estimated values for adequate intake in children have been interpolated from the known ranges in infants and adults with reference to nutrient density.

The level of adequate selenium intake in pregnant and lactating women is still a matter of scientific debate.

The efficacy of selenium intakes in excess of the estimated values in preventing myocardial infarction, cancer or disorders of the immune system has not yet been sufficiently clarified [3, 5] (see section II, page 193). Intakes exceeding the estimated values therefore cannot be recommended.

No toxic effects have been observed after acute and after prolonged therapeutically indicated administration of 200 - 400 µg selenium per day under medical supervision. Whether, and to what extent, even higher therapeutic doses of selenium given for a short period in intensive-care medicine, surgery or radiation therapy will be beneficial or elicit toxic effects remains to be clarified in prospective controlled studies which have yet to be conducted. In adults signs of chronic selenium intoxication have been observed at daily doses of 800 µg selenium and more [21].

References

[1] Abdulla, M., Behbehani, A., Dashti, H.: Dietary intake and bioavailability of trace elements. Biol. Trace Elem. Res. 21 (1989), 173-178

[2] Behne, D., Kyriakopoulos, A.: Neue Selenoproteine: Verteilung, Funktionen und Selenbedarf. In: Spurenelemente. I. Lombeck (ed.), Wiss. Verlagsges., Stuttgart (1997)

[3] Biesalski, H. K. et al: Kenntnisstand Selen - Ergebnisse des Hohenheimer Konsensusmeetings. Akt. Ernähr.-Med. 22 (1997), 224-231

[4] Chen, X., Yang, G., Chen, J., Wen, Z., Ge, K.: Studies on the relations of selenium and Keshan Disease. Biol. Trace Element Res. 2 (1980), 91-107

[5] Clark, L. C. et al: Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. JAMA 276 (1996), 1957-1963

[6] Drobner, C., Anke, M., Thomas, G.: Selenversorgung und Selenbilanz Erwachsener in Deutschland. In: Mengen- und Spurenelemente (16. Arbeitstagung), Anke, M. et al. (eds.), H. Schubert, Leipzig (1996), 627-634

[7] Duffield, A. J., Thomson, C. D., Hill, K. E., Williams, S.: An estimation of selenium requirements for New Zealanders. Am. J. Clin. Nutr. 70 (1999), 896-903

[8] Köhrle, J.: Thyorid hormone deiodination in target tissues – a regulatory role for the trace element selenium? Exp. Clin. Endocrinol. 102 (1994), 63-89

[9] Levander, O. A., Whanger, P. D.: Deliberations and evaluations of the approaches, endpoints and paradigms for selenium and iodine dietary recommendations. J. Nutr. 126 (1996), 2427S-2434S

[10] Lombeck, I., Jochum, F., Terwolbeck, K.: Selenium status in infants and children with phenylketonuria and in maternal phenylketonuria. Eur. J. Pediatr. 155 (1996) Suppl. 1, 140-144

[11] Oster, O., Prellwitz, W.: The daily dietary selenium intake of West German adults. Biol. Trace Elem. Res. 20 (1989), 1-14

[12] Oster, O., Schlinke, B., Marks, U.: Der Selenstatus von Vegetariern und Nichtvegetariern in der Bundesrepublik Deutschland. Z. Ernährungswiss. 34 (1995), 62

[13] Pelus, E., Arnaud, J., Ducros, V.: Trace element (Cu, Zn, Fe, Mn, Se) intakes of a group of French men using the duplicate portion technique. Int. J. Food Sci. Nutr. 45 (1994), 63-70

[14] Pfannhauser, W.: Das essentielle Spurenelement Selen: Bedeutung, Wirkung und Vorkommen in der Ernährung. ernährung/nutrition 16 (1992), 642-646

[15] Robinson, M. F., Thomson, C. D.: The role of selenium in the diet. Nutr. Abstr. Rev. 53 (1983), 3-26

[16] Roekens, E. J., Robberecht, H. J., Deelstra, H. A.: Dietary selenium intake in Belgium for different population groups at risk for deficiency. Z. Lebensm. Unters. Forsch. 182 (1986), 8-13

[17] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific publishers, Stuttgart (2000)

[18] Sunde, R. A.: Selenium. In: Handbook of nutritionally essential mineral elements. O'Dell, B. L., Sunde, R. A., (eds.), Marcel Dekker Inc., New York (1997), 493-556

[19] Vanderpas, J. B., Contempré, B., Duale, N. L. et al.: Selenium deficiency mitigates hypothyroxinemia in iodine-deficient subjects. Am. J. Clin. Nutr. 57 (1993), 271S-275S

[20] World Health Organization: Trace Elements in Human Nutrition and Health. WHO, Geneva (1996)

[21] Yang, G., Yin, S., Zhou, R. et al.: Studies of safe maximal daily dietary Se-intake in a seleniferous area in China. Part II. Relation between Se-intake and the manifestation of clinical signs and certain biochemical alterations in blood and urine. J. Trace Elem. Electrolytes Health Dis. 3 (1989), 123-130

[22] Zimmerli, B., Haldimann, M., Sieber, R.: Selenversorgung der schweizerischen Bevölkerung. In: Vierter Schweizerischer Ernährungsbericht. Bundesamt für Gesundheit (ed.), Bern (1998), 74-86

Copper, Manganese, Chromium, Molybdenum

A. Estimated values for adequate intake

Age	Copper mg/day	Manganese mg/day	Chromium µg/day	Molybdenum µg/day
Infants				
0 to under 4 months	0.2-0.6	—[1]	1- 10	7
4 to under 12 months	0.6-0.7	0.6-1.0	20- 40	20- 40
Children				
1 to under 4 years	0.5-1.0	1.0-1.5	20- 60	25- 50
4 to under 7 years	0.5-1.0	1.5-2.0	20- 80	30- 75
7 to under 10 years	1.0-1.5	2.0-3.0	20-100	40- 80
10 to under 15 years	1.0-1.5	2.0-5.0	20-100	50-100
Adolescents and adults	1.0-1.5	2.0-5.0	30-100	50-100

[1] No data available; see text pages 184 and 185

B. Explanations

Copper

The average copper content of the human body is 80 - 100 mg. Copper is a constituent of several metalloenzymes, most of which belong to the endogenous antioxidative system. Copper has an essential function as part of ceruloplasmin, the most important transport protein for copper. It catalyzes oxidation of bivalent iron which is the stored iron form, to trivalent iron which is subsequently bound to transferrin. Thus copper is involved in iron metabolism.

Insufficient intake of copper may cause hypochromic microcytic anaemia despite high iron concentrations in the liver. Other symptoms of copper deficiency are leucocytopenia, granulocytopenia, occurrence of bone fractures due to osteoporosis, spontaneous vascular ruptures and aneurysms because of a disturbed synthesis of collagen and elastin, reduced pigmentation of hair and skin, and, at the advanced stage, neurological disorders. Blood loss is always accompanied by loss of copper. Characteristics of copper deficiency, furthermore, are found in the kinky-hair syndrome, a rare hereditary disturbance in copper metabolism which does not respond to copper supplementation and is already fatal in infants [23].

In adults, about 1.25 mg of copper per day are sufficient to replace faecal and urinary losses [19]. WHO estimates the average requirement at 11 µg/kg of body weight [29]. The Population Reference Intake specified by the Scientific Committee for Food (SCF) is 1.1 mg of copper per day [9]. Estimated values for adequate intake, according to the results of investigations, are in the range of 1.0 - 1.5 mg of copper per day. In Germany, where copper intake has increased in the last 10 years, the average daily dietary intake in 1996 was 1.1 mg in women and 1.2 mg in men [5].

Copper concentrations in human milk decrease from 0.6 to 0.2 mg per litre during the first six months post partum. An exclusively breast-fed infant receives about 60 µg of copper per kg body weight per day on average. The infant's requirement for copper during the first months of life is solely met by breast milk [10]; this is due to fetal copper stores in the newborn's liver [28] and to the high absorption rate.

Good sources of copper are cereal products, innards (liver), fish, crustaceae, nuts, cocoa, chocolate, coffee, tea and some green vegetables. Copper bioavailability varies between 35 and 70% [9, 12].

High copper concentrations in drinking water (> 10 mg/l) have been associated with liver damage in infants, so-called early infantile liver cirrhosis [15]. For reasons of health, copper tubes must not be used for well water with a pH of < 7.3. Copper concentrations should be below 2 mg/l water in order to avoid potential injury.

Manganese

The human body contains about 10 - 40 mg of manganese. Relatively high manganese concentrations are found in bones. Among manganese metalloenzymes are pyruvate carboxylase, manganese-superoxide-dismutase, and glycosyltransferase; the latter catalyzes proteoglycan synthesis in cartilaginous tissue and in epiphyseal growth plates. In addition, manganese activates many other enzymes, mostly non-specifically.

So far, signs of manganese deficiency in humans have only been reported in some individuals on total parenteral nutrition. In other species, signs of manganese deficiency have included delayed growth, skeletal abnormalities, disturbed or depressed reproductive function, severe neurological disorders in newborns and defects in lipid and carbohydrate metabolism.

Neither a deficiency nor overdosage is assumed to occur at an intake of 2 - 5 mg manganese per day in adults [27]. From balance studies, however, a requirement of 0.74 mg per day has also been derived [13] which secures all physiological functions, but allows for no body reserves. Data on manganese requirement in humans are still unsatisfactory; hence only estimated values for adequate intake are given.

Analyses of total diets in Germany and in the USA yielded an average daily manganese intake of 2.7 mg in men and 2.4 mg in women [5, 21].

Breast milk, with about 7 - 14 µg of manganese per litre [25], contains only low manganese concentrations. Predominantly positive manganese balances have nevertheless been found in breast-fed infants [11]. Manganese intake increases considerably when supplementary food *(Beikost)* is introduced into the infant's diet. Infants at the age of six and twelve months have been found to ingest average daily doses of 71 and 80 µg, respectively, per kg body weight [14]. These data provided the basis for the estimated values for adequate manganese intake during the first year of life. Estimated values for children and adolescents were derived by extrapolation on the basis of body weight and assumed food intake.

Food of vegetable origin contains more manganese than animal food. Good sources are tea, leek, lettuce, spinach, strawberries and oat flakes.

Manganese, if ingested in large quantities, is toxic. A toxic threshold value cannot be indicated, however. Intoxications caused by manganese-containing food have not been reported. In children on prolonged artificial nutrition neurological disorders have been observed after intravenous administration of manganese in combination with zinc and copper.

Chromium

Chromium is actively involved in carbohydrate metabolism, even though the structure of a postulated glucose tolerance factor remains to be elucidated. Chromium intakes < 20 µg per day impair glucose tolerance. Clinical signs of chromium deficiency including insulin-resistant hyperglycaemia, hyperlipidaemia, weight loss, peripheral neuropathy and ataxia have only been observed after prolonged parenteral nutrition [6]. Intravenous administration of trivalent chromium corrected the deficiency. In patients with disturbed glucose tolerance and low chromium intake, supplementation with chromium enhanced carbohydrate metabolism [4].

The absorption rate of dietary chromium is usually about 0.5%, maximally 3%. US Americans ingest on average less than 50 µg of chromium per day [3, 18, 20]

without known signs of deficiency. In Germany dietary chromium intake measured in duplicate studies was 61 ± 31 µg/day in women and 84 ± 55 µg/day in men [5]. Lactating women, however, showed a moderately negative balance; it was corrected after the lactation period by high levels of dietary chromium.

WHO has estimated adult requirement at 20 µg of chromium per day. This amount secures all physiological functions but no body reserves [29]. Adding a certain requirement for body reserves one arrives, in the absence of satisfactory data, at an estimated value for adequate intake in adults of 30 - 100 µg of chromium per day.

Although the chromium content in breast milk may be low (0.18 µg/l) [2], breast-fed infants are adequately supplied. In view of the low absorption rate, estimated values for adequate chromium intake extend over a relatively wide range. Estimated values for infants and children have been extrapolated assuming equally wide relative ranges and age-related energy intakes.

Appreciable quantities of chromium are contained in meat, liver and eggs, and also in oat flakes, tomatoes, lettuce, cocoa and mushrooms.

No abnormalities have been observed even after chronic intake of 200 µg of chromium per day. Toxicity of dietary trivalent chromium is very low, in contrast to the toxicity of the occupational hazard; hexavalent chromium dusts containing it are known to be carcinogenic.

Molybdenum

Molybdenum is a constituent of the enzymes xanthine oxidase, sulphite oxidase, and aldehyde oxidase. For the latter, a compound of molybdenum and pterine is a cofactor. A cariostatic effect of molybdenum has also been suggested.

So far, signs of molybdenum deficiency have only been observed in patients on prolonged parenteral nutrition [1, 22]. The molybdenum-pterine cofactor is involved in a rare hereditary metabolic disorder [22]. Common to all cases of molybdenum deficiency was an impairment of the metabolism of sulphur amino acids and nucleotides as well as functional disorders of nerves and brain.

The absorption rate of molybdenum is high; about 80%. In recent well controlled balance studies 4 healthy young men who ingested 22 µg of molybdenum per day over 102 days showed no clinical signs of deficiency [26] but functional losses of molybdenum-dependent enzymes could not be excluded [8]. In Germany in the last few years intake of molybdenum from mixed diets has increased to 89 µg/day in women and 100 µg/day in men [16]. The concentration

of molybdenum in colostrum is 15 µg/l but decreases rapidly to 1 - 2 µg/l in mature breast milk [7]. Formula-fed infants under 3 months ingest more than 6 µg of molybdenum per day from adapted infant formulae and 12 - 27 µg per day from partly adapted infant formulae [17].

In view of the lack of satisfactory data, adequate intake of molybdenum has been estimated at 50 - 100 µg per day in adults. Estimated values for infants [24] and children have been extrapolated in the same way as for chromium.

Good sources of molybdenum are pulses (peas, lentils, beans) and cereals.

Long-term exposure, due to environmental conditions, to extremely high intakes of molybdenum (10 - 15 mg per day) has been assumed to cause symptoms characteristic of gout. Increased renal copper excretion has also been recorded. The risk of copper depletion due to increased intake of molybdenum therefore cannot be excluded.

Other trace elements

Our present state of knowledge gives reason to assume that other trace elements such as cobalt and nickel could as well be components or activators of essential compounds (proteins, hormones, enzymes or other functionally important substances).

Cobalt which is a constituent of vitamin B_{12} is capable of non-specifically activating several enzymes. It is only essential as part of vitamin B_{12}. A deficiency of vitamin B_{12} cannot be corrected by cobalt supplementation. An estimated value for adequate intake therefore is neither possible nor necessary. Excessive intakes of inorganic cobalt have been reported to produce cardiac muscle damage in humans.

Nickel is (by definition) also a trace element. For nickel, as for manganese and molybdenum, signs of deficiency in humans have not been reported so far because there are sufficient quantities of this element in food to meet human requirements. Exceptions are individuals on parenteral nutrition not containing these trace elements, or subjects with genetic defects. Humans contain 0.5 mg of nickel. Adequate intakes have been estimated at 25 - 30 µg per day [29].

References

[1] Abumrad, N. N., Schneider, A. J., Steel, D., Rogers, L. S.: Amino acid intolerance during prolonged total parenteral nutrition reversed by molybdate therapy. Am. J. Clin. Nutr. 34 (1981), 2551-2559

[2] Anderson, R. A., Bryden, N. A., Patterson, K. Y., Veillon, C., Andor, M. B., Moser-Veillon, P. B.: Breast milk chromium and its association with chromium intake, chromium excretion and serum chromium. Am. J. Clin. Nutr. 57 (1993), 519-523

[3] Anderson, R. A., Bryden, N. A., Polansky, M. M.: Dietary intake of calcium, chromium, copper, iron, magnesium, manganese, and zinc: duplicate plate values corrected using derived nutrient intake. J. Am. Diet. Assoc. 93 (1993), 462-464

[4] Anderson, R. A.: Chromium, glucose intolerance and diabetes. J. Am. Coll. Nutr. 17 (1998), 548-555

[5] Anke, M., Glei, M., Groppel, B., Rother, C., Gonzales, D.: Mengen-, Spuren- und Ultraspurenelemente in der Nahrungskette. Nova Acta Leopoldina 79 (1998), 157-190

[6] Brown, R. O., Forloines-Lynn, S., Cross, R. E., Heizer, W. D.: Chromium deficiency after long-term total parenteral nutrition. Dig. Dis. Sci. 31 (1986), 661-664

[7] Casey, C. E., Neville, M. C.: Studies in human lactation 3: molybdenum and nickel in human milk during the first month of lactation. Am. J. Clin. Nutr. 45 (1987), 921-926

[8] Chiang, G., Swendseid, M. E., Turnlund, J. R.: Studies of biochemical markers indicating molybdenum status in humans. FASEB J. 3 (1989), A1073

[9] Commission of the European Communities: Reports of the Scientific Committee for Food. Nutrient and energy intakes for the European Community. Thirty-first series. Zinc, Copper. Office for Official Publications of the European Communities, Luxemburg (1993)

[10] Dörner, K., Dziadzka, S., Hohn, A., Oldigs, H. D., Schulz-Lell, G., Schaub, J.: Longitudinal manganese and copper balances in young infants and preterm infants fed on breast-milk and adapted cow's milk formulas. Br. J. Nutr. 61 (1989), 559-572

[11] Dörner, K., Dziadzka, S., Sievers, E.: Manganbilanzen beim Menschen. In: Spurenelemente und Ernährung. Wolfram, G., Kirchgeßner, M. (eds.), Wissenschaftliche Verlagsgesellschaft, Stuttgart (1990), 123-134

[12] Fairweather-Tait, S. J.: Bioavailability of copper. Eur. J. Clin. Nutr. 51 (1997), S24-S26

[13] Freeland-Graves, J. H., Behmardi, F., Bales, C. W., Dougherty, V., Lin, P. H., Crosby, J. B., Trickett, P. C.: Metabolic balance of manganese in young men consuming diets containing five levels of dietary manganese. J. Nutr. 118 (1988), 764-773

[14] Gibson, R. S., De Wolfe, M. S.: The dietary trace metal intake of some Canadian full-term and low birthweight infants during the first twelve months of infancy. J. Can. Diet. Assoc. 41 (1980), 206-215

[15] Hädrich, J.: Auffallend hohe Kupferkonzentrationen in Lebern von Mastkälbern. Deutsche Lebensmittel-Rundschau 92 (1996), 103-113

[16] Holzinger, S., Anke, M., Röhrig, B., Gonzalez, D.: Molybdenum intake of adults in Germany and Mexico. Analyst 123 (1998), 447-450

[17] Holzinger, S., Anke, M., Seeber, O., Jaritz, M.: Die Molybdänversorgung von Säuglingen und Erwachsenen. 18. Arbeitstagung Mengen- und Spurenelemente, Friedrich-Schiller-Universität Jena (1998), 916-923

[18] Hunt, C. D., Stoecker, B. J.: Deliberations and evaluations of the approaches, endpoints, and paradigms for boron, chromium and fluoride dietary recommendations. J. Nutr. 126 (1996), 2441S-2451S

[19] Klevay, L. M., Reck, S. J., Jacob, R. A., Logan, G. M. Jr., Munoz, J. M., Sandsteadt, H. H.: The human requirement for copper. I. Healthy men fed conventional American diets. Am. J. Clin. Nutr. 33 (1980), 45-50

[20] Offenbacher, E. G.: Chromium in the elderly. Biol. Trace Elem. Res. 32 (1992), 123-131

[21] Pennington, J. A., Young, B. E., Wilson, D. B.: Nutritional elements in U.S. diets: results from the Total Diet Study 1982 to 1986. J. Am. Diet. Assoc. 89 (1989), 659-664

[22] Rajagopalan, K. V.; Molybdenum: an essential trace element in human nutrition. Annu. Rev. Nutr. 8 (1988), 401-427

[23] Schümann, K., Classen, H. G., Dieter, H. H. et al.: Hohenheimer Konsensusgespräch Kupfer. Akt. Ernähr.-Med. 24 (1999), 283-296

[24] Sievers, E. et al: Der Molybdänbedarf im Säuglingsalter. In: Lombeck, I.: Spurenelemente - Bedarf, Vergiftungen, Wechselwirkungen und neuere Meßmethoden. Wissenschaftliche Verlagsgesellschaft, Stuttgart (1997)

[25] Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm, Scientific Publishers, Stuttgart (2000)

[26] Turnlund, J. R., Keyes, W. R., Peiffer, G. L., Chiang, G.: Molybdenum absorption, excretion, and retention studied with stable isotopes in young men during depletion and repletion. Am. J. Clin. Nutr. 61 (1995), 1102-1109

[27] Velazques, S.F., Du, J.T.: Derivation of the reference dose for manganese. In: Risk assessment of essential elements. Mertz, C., Abernathy, C., Olin, S.S. (eds.) International Life Science Institute Press, Washington DC (1994), 253-266

[28] Widdowson, E.M.: Trace elements in foetal and early postnatal development. Proc. Nutr. Soc. 33 (1974), 275-284

[29] World Health Organization: Trace elements in Human Nutrition and Health. WHO, Geneva (1996)

Ultratrace elements

Ultratrace elements have been defined as all other elements, the essentiality of which has been confirmed in animal experiments using semi-synthetic diets over several generations and for which signs of deficiency have occurred under these extreme conditions. Their special physiological functions are still unknown, however. Dietary intake of these elements, according to the present state of knowledge, obviously satisfies the requirements of animals (and humans) as pertinent signs of deficiency have so far not been reported. The detection of biochemical functions in essential tissues and organs would qualify them as trace elements.

Ultratrace elements comprise:

aluminium (Al)	antimony (Sb)	arsenic (As)	barium (Ba)
bismuth (Bi)	boron (B)	bromine (Br)	cadmium (Cd)
caesium (Cs)	germanium (Ge)	lead (Pb)	lithium (Li)
mercury (Hg)	rubidium (Rb)	samarium (Sm)	silicon (Si)
strontium (Sr)	thallium (Tl)	titanium (Ti)	tungsten (W)

All inorganic body constituents, if ingested in excess, may produce intoxication by blocking the action of essential compounds, entering into interactions with other elements, or initiating a re-distribution of essential compounds in the body and thus causing diseases.

Section II: Preventive aspects of nutrients and food components

In the Western world the risk of deficiency diseases has decreased considerably in the last few decades owing to diets mostly supplying too much energy but ensuring adequate intake of essential nutrients. This explains - at least in part - the continuous increase in mean life expectancy [54]. Statistics have shown that the incidence of degenerative diseases is also increasing [11]. They include different types of cancer, skeletal, muscular and connective tissue diseases as well as neurological and psychiatric disorders, not to forget a high incidence of cardiovascular diseases. This trend which is due to a larger proportion of older individuals in our society is also promoted by unfavourable dietary behaviour. Adverse effects of high-fat and high-energy diets have already been discussed in the chapter on 'Fat' (see page 37). A simple, but very efficient means of prevention is avoiding or lowering the classical risk factors for atherosclerosis (obesity, hypertension, diabetes mellitus, dyslipoproteinaemia) and for cancer (obesity, smoking, alcohol).

Epidemiological, biochemical and molecular-biological studies have furnished conclusive evidence for a relationship between the incidence and course of certain chronic diseases and dietary habits and lifestyle-associated factors. This underlines impressively that different food components, in addition to their nutritive value, have important 'preventive' properties. Dietary recommendations, accordingly, must also consider preventive aspects of nutrients.

In determining nutritive reference values scientists can rely on standard procedures (e.g. biochemical parameters of nutrient status or of nutrient doses preventing or correcting signs of deficiency). Furnishing evidence for the ability of nutrients to prevent health disorders in the long run is much more difficult. Usually, such protective effects are only detected in long-term studies under controlled conditions. Such studies, furthermore, require suitable and detectable biomarkers. *In vitro* studies and short-term interventions frequently provide information about potential mechanisms, but not about long-term effects. This also applies to probiotics.

The reliability of epidemiological studies increases from population studies through case-control studies and cohort studies up to randomized placebo-controlled intervention studies [9, 50]. Observational studies also include dietary epidemiology which provides important knowledge for formulating recommendations to the public [37].

In fact, satisfactory and reliable data on preventive effects have so far only been available for a few nutrients. Although epidemiological studies suggest a relationship

between diets and the risk of certain diseases, it is still unclear at present - except for some extremely rare cases - which food components are responsible for the effect.

Based on the most relevant literature, the role of selected nutrients in the prevention of different diseases will be discussed in the following section and, as far as possible, be combined with corresponding recommendations.

Compounds effective in the body's antioxidative protective system

Special importance for the prevention of chronic degenerative diseases has been attached to the antioxidative capacity of the human organism. The development and course of atherosclerosis or cancer, age-related macular degeneration, cataracts, inflammatory arthropathies, photo-ageing of the skin, and some other diseases are assumed to be caused by reactive oxygen species. Convincing evidence for the effectiveness of antioxidant supplementation has not been furnished in any of these diseases; so only atherosclerosis and cancer, those diseases most frequently listed in the statistics of the causes of death will be discussed.

Antioxidative capacity results from the total of endogenous and exogenous protective mechanisms, ensuring an equilibrium of pro- and antioxidants. It varies from individual to individual. Antioxidants may be of enzymatic or non-enzymatic nature. A nutritional protective effect implies that an impaired equilibrium between pro- and antioxidants (oxidative stress) can be corrected by intake of enzyme cofactors of the endogenous antioxidative enzymatic protective system (e.g. selenium, copper, manganese, zinc) or of antioxidants of the exogenous non-enzymatic protective system (ascorbic acid, tocopherols, carotenoids, flavonoids and other phytochemicals).

The imbalance is probably not corrected by a single antioxidant, but by intake of a mixture of different antioxidants present in food and predominantly in food of vegetable origin. Ascorbic acid for example is not only a water-soluble radical scavenger; it also serves the regeneration of vitamin E which, among other things, prevents lipids from being oxidized by virtue of its fat-soluble chain-breaking radical scavenger function. Synergisms of this kind have been found to exist also among other antioxidants.

A statistical analysis of retrospective and prospective epidemiological studies allows the conclusion that the risk of degenerative chronic diseases and of cardiovascular diseases and cancer in particular is reduced, in the sense of primary prevention, by early, regular and high consumption of vegetables, fruit and whole-grain cereal products [5, 47]. This effect is mainly attributed to the intake of natural antioxidants associated with such a dietary regimen, mainly

vitamin C, vitamin E, ß-carotene and selenium. There has been no scientific evidence, however, for a causal connection between isolated antioxidants, e.g. vitamin E or the cofactor selenium, and protection against myocardial infarction or cancer.

The finding, verified in numerous studies, that a high intake of vegetables, fruit and whole-grain cereal products is associated with a lower risk for cancer [5] gave reason to initiate comprehensive intervention studies which should document the effectiveness of individual food components in the primary prevention of cancer. Three large prospective placebo-controlled intervention studies in about 70,000 individuals could not demonstrate a reduced incidence of lung cancer or of cancer in general. Supplements of ß-carotene (20 - 30 mg per day), vitamin A (25,000 IU per day) and/or vitamin E (50 IU = 33.5 mg of α-tocopherol equivalents per day) were given either singly or in combination over 4 - 13 years [26, 40, 56]. Intervention studies using ß-carotene have been the most contradictory [40, 43, 56]. They give reason to assume that intake levels and plasma concentrations of ß-carotene are only indicators of vegetable consumption.

In the development of cancer, antioxidative protectants are, if at all, most effective at an early stage. Later their effect is unsatisfactory or actually promotes tumor growth. Unfavourable results obtained in one of these studies in a subgroup of smokers who received ß-carotene supplements, and the reason for discontinuing another in which ß-carotene and vitamin A were supplemented have been interpreted accordingly [40, 56]. Thus caution should be exercised in supplementing ß-carotene in the case of smokers [39]. ß-Carotene supplements fail to produce a protective effect against lung cancer; in smokers they have even been found to be detrimental with regard to the incidence of lung cancer and mortality [1].

Another intervention study in China in about 29,000 individuals whose diets were supplemented with ß-carotene, α-tocopherol and selenium succeeded in reducing mortality; this was due, among other things, to a 13% lower cancer incidence [6]. Because of the generally poor nutritional situation in the region concerned it has been doubted, however, whether these results are transferable to other countries, especially those with adequate nutrition.

Diets containing much vitamin C from fruit and vegetables are associated with a lower risk for cancer, especially of the oesophagus, stomach and colon. Intervention studies using vitamin C as a supplement failed to reduce the incidence of gastric and colonic cancer, however. Nor could the risk for coronary heart disease be reduced; the data on vitamin C were unconvincing [10, 36].

A relationship verified in several epidemiological studies between low plasma concentrations of antioxidative vitamins and a greater risk for coronary heart

diseases gave the impetus to carry out further investigations [18]. An additional analysis of one of the intervention studies against cancer for primary prevention of coronary heart diseases did not show any significant beneficial effect [44, 56]. Two large prospective observational studies may be interpreted in such a way that supplementation with daily doses > 100 IU of vitamin E (> 67 mg of α-tocopherol equivalents) over at least two years is accompanied by a reduction in myocardial infarction rate of > 30% [48, 52]. An influence of a previously poorer supply cannot be excluded, however. Shorter periods of supplementation and doses < 100 IU/day showed no beneficial effect [53].

So far, there has been no conclusive evidence for an effect, in the sense of primary prevention, against cancer or myocardial infarction in intervention studies in which antioxidative food components were administered, either singly or in combination, to adequately nourished populations. From this it has been concluded that the effect of antioxidants as found in epidemiological studies is confined to antioxidants in natural systems or in combination with other effective dietary components. This interpretation is supported by a prospective observational study in 34,000 postmenopausal women in whom supplementation with up to 250 IU of vitamin E and more (> 168 mg of α-tocopherol equivalents) per day over 7 years had no significant effect on the incidence of coronary deaths while a much lower dietary vitamin E intake (without supplement) showed an effect which depended on the amount of dietary vitamin E ingested [33].

Based on epidemiological data, certain plasma antioxidant concentrations in healthy adults have been regarded as guiding values for primary prevention of cancer and cardiovascular diseases. They have been derived from prospective studies and case studies and from comparisons of countries with large cohorts of test persons (e.g. the Basel study [13], US Health Professionals Study, NHANES, Edinburgh angina case study, WHO MONICA project). These plasma concentrations are: α-tocopherol > 30 µmol/l (lipid-corrected: 220 mg/dl cholesterol [5.7 mmol/l], 110 mg/dl triglycerides [1.3 mmol/l]), vitamin C > 50 µmol/l, and ß-carotene > 0.4 µmol/l [3]. For selenium, > 50 µg/l is regarded as a normal and desirable plasma concentration because at lower levels reduced activity of the glutathione peroxidase (GPx) function in the organism must be expected [4]. It has so far not been possible to delineate guidance values of a desirable plasma concentration for other phytochemicals with antioxidant action or for trace elements besides selenium which have a cofactor function in the enzymatic antioxidative system.

In 1995 a consensus conference specified daily intakes of 75 - 150 mg of vitamin C, 15 - 30 mg of vitamin E (α-tocopherol equivalents) and 2 - 4 mg of ß-carotene [3] for healthy individuals not exposed to oxidative stress to reach the above desirable plasma concentrations. The VERA study has shown that in Germany these daily intakes of the vitamins C and E and of ß-carotene and selenium are readily obtained in a normal diet [4, 28, 49].

It must be expected, however, that these guiding values of desirable plasma concentrations are not always achieved in, or are not sufficient for individual persons despite balanced nutritious diets. This may be due to the inter- and intraindividual variability of the dependence of plasma concentrations on intakes and to increased requirement caused by oxidative stress. In such special cases supplementation of antioxidative vitamins may be indicated upon medical advice (see page 12). Supplementation should not be used for compensation of an unbalanced diet or an unhealthy lifestyle. Excepted from this rule are older individuals, especially those living alone, who, because of their living conditions, subsist on imbalanced and inadequate diets. Because usually several nutrient deficits prevail in these cases balanced liquid formulae should be ingested between meals; this applies in particular to old persons who are sick (see pages 16 and 17).

Secondary prevention by antioxidants has been clearly defined in preventive medicine and focusses in patients with coronary heart disease on vitamin E. Out of several prospective intervention studies for secondary prevention [21, 45, 55], strictly speaking, only one, the double–blind, placebo–controlled CHAOS study conducted over 2 years showed that doses of 400 and 800 IU of vitamin E/day (about 270 and 540 mg of α-tocopherol equivalents) reduced the number of non-fatal myocardial infarctions. However, the number of fatal infarctions and cardiovascular mortality were as little influenced in this study [55] as they were in another in which 75 IU (50 mg of α-tocopherol equivalents) per day were given [45]. Also the most recent study of this kind using 450 IU (300 mg of α-tocopherol equivalents) was not successful in preventing coronary heart disease [21]. Numerous repeated claims that high-dose supplements prevent heart disease had already been critically addressed and questioned [24, 25].

By a meta-analysis of the results of all descriptive, case-control, prospective and randomized double-blind and placebo-controlled studies an attempt was made to clarify the possible role of vitamin E in preventing the manifestation and progression of atherosclerotic heart disease by different mechanisms [12]. Establishing a relationship between LDL oxidation and atherosclerosis was problematic. Later, in a critical evaluation of the large intervention studies (Physicians Health, CHAOS and ATBC study) the effectiveness of secondary prevention in coronary heart disease patients was even questioned in principle [46]. This scepticism is supported by a more recent prospective study in men at high risk for coronary heart disease [14] in whom a relationship between plasma concentrations of fat-soluble antioxidants (vitamins A and E, carotenoids) and the frequency of myocardial infarction was not observed.

The biochemical and pathophysiological knowledge accumulated so far demonstrates the need for antioxidative protection. The preventive effect of antioxidants administered either as isolated substances or in certain combinations still remains to be verified in further intervention studies [34]. Today's

knowledge of synergisms among antioxidative compounds rather speaks for ingesting them along with a balanced mixed diet. For these reasons preventive doses of antioxidative food components are not shown here; instead, the effectiveness of a balanced mixed diet and of a healthy lifestyle is underlined.

The therapeutic use of antioxidants in pharmacological doses and the administration of antioxidants in high-dose preparations for secondary prevention of myocardial infarction as well as the indications and control of effectiveness are matters for the medical profession.

Phytochemicals

Recent studies in different experimental and mostly *in vitro* systems have shown bioactive substances in plant foods to have many physiological and pharmacological effects [57]. These findings are supported by data obtained in epidemiological studies on the protective effect of diets rich in whole-grain products and in fruit and vegetables in particular. The importance of dietary fibre in these foods is pointed out on pages 51 and 52.

For some phytochemicals, plasma and urine concentrations in humans have been found to correlate with a lower risk for tumor and cardiovascular diseases [22, 29, 42]. The physiological effects ascertained and a potential preventive role in tumorigenesis have raised the question whether guiding values or estimated values for intake of phytochemicals should be established as well [23, 31, 58]. Signs of deficiency following inadequate intake of phytochemicals, in contrast to essential nutrients, have not been reported. The National Academy of Sciences of the United States (Institute of Medicine, Panel on Dietary Antioxidants) has released a DRI for ß-carotene as the first phytochemical [2]. This is not possible for other phytochemicals such as flavonoids and phytooestrogens in view of the lack of satisfactory data. The German Nutrition Society released a guiding value for ß-carotene as far back as 1991 (see also page 62).

Phytochemicals may be subdivided into different groups according to their chemical structure and functional properties [57]. The most important of these are carotenoids, phytosterols, glucosinolates, flavonoids, phenolic acids, protease inhibitors, monoterpenes, phytooestrogens, and sulphur compounds.

Depending on the diet, up to 14 carotenoids may be present in the blood of humans, among which ß-carotene and lycopene prevail. The total daily intake of carotenoids is about 6 mg. In epidemiological studies a diet rich in high-carotenoid fruit and vegetables correlated with a reduced risk for cardiovascular diseases and cancer. Carotenoids had anti-carcinogenic action in animal experiments; this could be due to antioxidative and immunomodulatory mechanisms.

However, in intervention studies 20 mg of ß-carotene per day failed to reduce the risk of cancer [26, 40, 56].

Phytosterols, which are found in nuts and seeds, differ in their chemical structure from cholesterol by an additional side chain. Because of this similarity they interfere with absorption of cholesterol in the small intestine. A daily intake of 1.5 - 3 g of phytosterols in the form of sandwich spread (10 times the average dietary content) can lower plasma cholesterol concentration by about 10%; however, it also reduces absorption of carotenoids.

Glucosinolates are found in all cruciferous vegetables (e.g. all cabbage species, radish, mustard). Their degradation leads to sulfur-containing isothiocyanates and to indoles. Many epidemiological studies have shown an inverse correlation between the intake of cabbage vegetables and the risk of cancer. In cell-culture systems and in animal and human studies an activation of carcinogen-detoxifying enzymes has been shown [57].

Flavonoids comprise about 5000 different phenolic compounds which are present in the majority of dietary plants. Their spectrum of action is wider than that of other phytochemicals. Their antioxidative action probably inhibits the development of atherosclerosis and cancer. This assumption is supported first by results of epidemiological studies on the relationship between flavonoid intake and the incidence of myocardial infarction [27, 32]. Flavonoids, furthermore, could also interfere with cancer development by other demonstrated mechanisms (e.g. regulation of cellular growth) [57]. Immunomodulatory effects of flavonoids observed in different experimental systems have not been sufficiently investigated in humans.

Protease inhibitors from dietary plants reduce the activity of physiological proteases (e.g. trypsin). They have been assumed to have anticancer effect. Their mechanisms of action (e.g. inhibition of tumor-specific proteases) differ from those of other phytochemicals. Protease inhibitors have also been assumed to show antioxidative action.

Monoterpenes, e.g. menthol or limonene, are potential anticancer substances. They can, according to experimental findings, interfere with the regulation of cellular growth (proliferation) e.g. by reducing the formation of cellular growth-promoting compounds.

Phytooestrogens bind to the same receptors as body oestrogens, however, with a substantially lower hormonal effect. Theoretically, they could interfere with carcinogenesis, especially of breast and prostate cancer, and favourably influence cardiovascular diseases and osteoporosis.

Sulphides such as allicin are contained in garlic and other plants of the onion family. *In vitro*, they have antimicrobial, anticancer, antioxidative and anti-inflammatory effects. There has also been evidence suggesting an influence on blood pressure and the immune system [57].

For many phytochemicals satisfactory data on their content in food, bioavailability, transport and metabolization are not available. Their mechanisms of action are, at best, only partly elucidated and criteria for optimal intake are not known. Some of them have also been shown to exhibit toxic effects as a function of their concentration. The fundamental importance of setting upper limits to the beneficial dietary intake for isolated phytochemicals has been exemplified by ß-carotene [39]. At present, however, neither recommendations nor limitations of intake can be scientifically substantiated.

It is undisputed, however, that phytochemicals play a part in the protective effect of high fruit and vegetable intake. The World Cancer Research Fund/American Institute for Cancer Research recommend that at least 7% of the calories needed for energy should be provided by fruit and vegetables [58]. Given a reference value for energy input of 8.5 MJ (2000 kcal) this would correspond to 400 g of fruit and vegetables per day. A diet rich in fruit and vegetables provides phytochemicals, complex carbohydrates, vitamins, minerals and dietary fibre but usually little fat. The German Nutrition Society, therefore, recommends ingestion of about 400 g of vegetables and 250 - 300 g of fruit per day. Fruit and vegetables should be consumed 5 times per day ideally along with meals but also in between meals. The recommendations for vegetables exceed those for fruit because epidemiological studies have shown vegetables to have a greater protective potential than fruit. The great variety of vegetables, fruit and whole-grain cereal products should be used to benefit from the numerous phytochemicals they contain [17, 51, 59]. This could probably reduce the risk of certain neoplastic diseases and coronary heart disease [19, 35].

It is not advisable to take food supplements containing phytochemicals in concentrated form as a substitute for a diet rich in fruit and vegetables. The bioavailability of phytochemicals from food supplements has scarcely been investigated. In addition, it is not known which phytochemicals if taken singly show preventive action and in what quantities.

Folate / folic acid

Numerous epidemiological investigations and case-control studies in particular have shown that increased plasma homocysteine concentrations are associated with a higher risk for atherosclerosis and that hyperhomocysteinaemia is an independent risk factor for myocardial infarction [7]. A threshold or guiding value

for the plasma homocysteine concentration cannot be unequivocally defined, however. The range suggested varies from 16 µmol/l to 10 µmol/l.

Metabolic and epidemiological studies have furnished evidence that plasma homocysteine concentrations are inversely proportional to blood folate concentrations. This is due to the fact that given a low folate concentration not enough methyl groups are available to convert homocysteine to methionine. The importance of two different genotypes of an enzyme involved has not been clarified [38]. Besides folate, vitamins B_6 and B_{12} also affect methionine metabolism.

Furthermore, many investigations have shown an inverse correlation between folate status and the occurrence of colorectal and (to a lesser extent) other tumors [16, 20]. The results of published studies do not provide conclusive evidence, however, that increased folate, vitamin B_6 and vitamin B_{12} intake lowers the risk for cancer and cardiovascular diseases [38].

Uncontroversial, however, are prophylactic recommendations (beyond the nutritive ones) for a pharmacological supplementation of the diet with folic acid to prevent fetal neural tube defects. Women planning a pregnancy or capable of becoming pregnant should ingest 0.4 mg of supplementary folic acid per day already before conception through the first trimester to prevent neural tube defects. Women who have a child with a neural tube defect and who are planning another pregnancy are advised to take 4.0 mg of folic acid per day before conception in order to prevent a neural tube defect in the next child.

Vitamin K

Recently, evidence has been mounting that vitamin K plays an active part in the development of skeletal strength. Vitamin K has a cofactor function in the γ-carboxylation of glutamyl residues in several bone proteins, including osteocalcin. Elevated serum levels of undercarboxylated osteocalcin and low serum vitamin K concentrations are associated with reduced bone density and increased risk for hip fractures. In more than 70,000 women aged 38 - 63 years participating in the prospective Nurses Health Study a significantly lower risk for hip fractures was found with adequate intake of vitamin K [15]. This finding correlated with the intake of one or more portions of salad per day. In a double-blind placebo-controlled intervention study with 90 mg of vitamin K_2 (menatetrenone) per day administered to 39 patients with osteoporosis bone density increased by 2.2% while it decreased by 7.3% in the placebo group within 24 weeks [41]. Further intervention studies in larger samples over a prolonged time are necessary to confirm these indications of a vitamin K effect in preventing osteoporosis.

Conclusions

It becomes obvious from these observations that the goal, described earlier in this chapter, to correlate different preventive effects on health disorders with individual nutrients and food components has not yet been accomplished. There are many indications indeed, especially those relating to antioxidative vitamins, but no conclusive results of intervention studies substantiating recommendations for the intake of individual nutrients. Placebo-controlled intervention studies in healthy test persons over prolonged periods of time are hardly feasible. Therefore, biomarkers for certain diseases which permit an assessment to be made after a reasonably short time are being sought. As little is known about such biomarkers and because of the need of their careful validation it will probably be a while before safe conclusions can be drawn. Without doubt, it will also be necessary to focus attention not only on individual nutrients, but also on combinations of nutrients as studies have shown that protective effects involve the concurrent and synergistic action of several nutrients.

Uncontroversial is, however, that a diet rich in fruit and vegetables fully complies with the demand for preventive and health promoting nutrition. The supply with antioxidative, immunologically positively evaluated nutrients is clearly enhanced by diets composed of food of predominantly vegetable origin. Underlined should be the immense diversity of nutrients which can be assumed to be responsible for the protective actions observed. Investigations have shown, however, that in Austria, Switzerland and Germany the recommendation to eat more fruit and vegetables is not being complied with [8, 11, 30]. For Germany an intake of only 290 g of fruit and vegetables has been found instead of 650 g as advised by DGE. Further efforts must be taken e.g. by educational campaigns ('5 a day') to convince the public of the benefits involved making a change in one's dietary behaviour worthwhile and encouraging consumption of healthful diets.

The possibility of enhancing nutrient supply, especially in risk groups, by nutrient-fortified and functional food is also being discussed. But in view of today's knowledge it makes little sense to ingest individual nutrients in high doses. This is underlined by the fact that too little is known about potential side-effects caused by high dosages.

References

[1] Albanes, D.: β-carotene and lung cancer: a case study. Am. J. Clin. Nutr. 69 (suppl) (1999), S1345-S1350

[2] Anonymous: Institute of Medicine releases DRIs for antioxidants and related compounds. J. Amer. Diet. Assoc. 98 (1998), 1411

[3] Biesalski, H. K.: Antioxidative Vitamine in der Prävention. Dt. Ärztebl. 92 (1995), A-1316-1321

[4] Biesalski, H. K.: Kenntnisstand Selen - Ergebnisse des Hohenheimer Konsensusmeetings. Akt. Ernähr.-Med. 22 (1997), 224-231

[5] Block, G., Patterson, B., Subar, A.: Fruit, vegetables and cancer prevention: a review of the epidemiological evidence. Nutr. Cancer 18 (1992), 1-29

[6] Blot, W. J., Li, J. Y., Taylor, P. R. et al.: Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. J. Natl. Cancer Inst. 85 (1993), 1483-1492

[7] Boushey, C. J., Beresford, S. A., Omenn, G. S., Motulsky, A. G.: A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 274 (1995), 1049-1057

[8] Bundesamt für Gesundheit (Hrsg.): Vierter Schweizerischer Ernährungsbericht. Bern (1998), 2-50

[9] Byers, T.: The role of epidemiology in developing nutritional recommendations: past, present, and future. Am. J. Clin. Nutr. 69 (suppl) (1999), S1304-S1308

[10] Carr, A. C., Frei, B.: Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. Am. J. Clin. Nutr. 69 (1999), 1086-1107

[11] Deutsche Gesellschaft für Ernährung (ed.): Ernährungsbericht 1996. Druckerei Henrich, Frankfurt/M. (1996)

[12] Diaz, M. N., Frei, B., Vita, J. A., Keaney, J. F. Jr.: Antioxidants and atherosclerotic heart disease. N. Engl. J. Med. 337 (1997), 408-416

[13] Eichholzer, M., Stähelin, H. B., Gey, K. F. et al.: Prediction of male cancer mortality by plasma levels of interacting vitamins: 17-year follow-up of the prospective Basel study. Int. J. Cancer 66 (1996), 145-150

[14] Evans, R. W., Shaten, B. J., Day, B. W., Kuller, L. H.: Prospective association between lipid soluble antioxidants and coronary heart disease in men: The Multiple Risk Factor Intervention Trial. Am. J. Epidemiol. 147 (1998), 180-186

[15] Feskanich, D., Weber, P., Willett, W. C., Rockett, H., Booth, S. L., Colditz, G. A.: Vitamin K intake and hip fractures in women: a prospective study. Am. J. Clin. Nutr. 69 (1999), 74-79

[16] Food and Nutrition Board/Institute of Medicine: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington D.C. (1998), 264-266

[17] Franceschi, S., Favero, A., LaVecchia, C., Negri, E., DalMaso, L., Salvini, S., Decarli, A., Giacosa, A.: Influence of food groups and food diversity on breast cancer risk in Italy. Int. J. Cancer 63 (1995), 785-789

[18] Gey, K. F., Moser, U. K., Jordan, P., Stähelin, H. B., Eichholzer, M., Lüdin, E.: Increased risk of cardiovascular disease at suboptimal plasma concentrations of essential antioxidants: an epidemiological update with special attention to carotene and vitamin C. Am. J. Clin. Nutr. 57 (suppl) (1993), S787-S797

[19] Gillman, M. W., Cupples, L. A., Gagnon, D., Posner, B. M., Ellison, R. C., Castelli, W. P., Wolf, P. A.: Protective effects of fruits and vegetables on development of stroke in men. JAMA 273 (1995), 1113-1117

[20] Giovannucci, E., Stamper, M. J., Colditz, G. A., Hunter, D. J., Fuchs, C. H., Rosner, B. A., Speizer, E., Willett, W. C.: Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. Ann. Intern. Med. 129 (1998), 517-524

[21] GISSI-Prevenzione Investigators: Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 354 (1999), 447-455

[22] Greenberg, E. R., Baron, J. A., Karagas, M. R., Stukel, T. A., Nierenberg, D. W., Stevens, M. M., Mandel, J. S., Haile, R. W.: Mortality associated with low plasma concentration of beta carotene and the effect of oral supplementation. JAMA 275 (1996), 699-703

[23] Hendrich, S., Lee, K. W., Xu, X., Wang, H. J., Murphy, P. A.: Defining food components as new nutrients. J. Nutr. 124 (1994), 1789S-1792S

[24] Hennekens, C. H., Buring, J. E., Peto, R.: Antioxidant vitamins - benefits not yet proved. N. Engl. J. Med. 330 (1994), 1080-1081

[25] Hennekens, C. H., Gaziano, J. M., Manson, J. E., Buring, J. E.: Antioxidant vitamin-cardiovascular disease hypothesis is still promising, but still unproven: the need for randomized trials. Am. J. Clin. Nutr. 62 (suppl) (1995), 1377S-1380S

[26] Hennekens, C. H., Buring, J. E., Manson, J. E. et al.: Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. N. Engl. J. Med. 334 (1996), 1145-1149

[27] Hertog, M. G., Kromhout, D., Aravanis, C., Blackburn, H., Buzina, R. et al: Flavonoid intake and long-term risk of coronary heart disease and cancer in the seven countries study. Arch. Intern. Med. 155 (1995), 381-386

[28] Heseker, H., Schneider, R., Moch, K. J., Kohlmeier, M., Kübler, W.: Vitaminversorgung in der Bundesrepublik Deutschland. In: Kübler, W., Anders, H., J., Heeschen, W., Kohlmeier, M.: VERA-Schriftenreihe Bd. IV, Wiss. Fachverlag Dr. Fleck, Niederkleen (1992)

[29] Ingram, D., Sanders, K., Kolybaba, M., Lopez, D.: Case-control study of phyto-oestrogens and breast cancer. Lancet 350 (1997), 990-994

[30] Institut für Ernährungswissenschaften der Universität Wien (ed.); im Auftrag des Bundesministeriums für Frauenangelegenheiten und Verbraucherschutz und des Bundesministeriums für Arbeit, Soziales und Gesundheit: Österreichischer Ernährungsbericht 1998. Wien (1998), 11-16

[31] Johnson, I. I., Williamson, G., Musk, S. R. R.: Anticarcinogenic factors in plant foods: a new class of nutrients? Nutr. Res. Rev. 7 (1994), 175-204

[32] Katan, M. B.: Flavonoids and heart disease. Am. J. Clin. Nutr. 65 (1997), 1542-1543

[33] Kushi, L. H., Folsom, A. R., Prineas, R. J., Mink, P. J., Wu Y., Bostick, R. M.: Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. N. Engl. J. Med. 334 (1996), 1156-1162

[34] Kushi, L. H.: Vitamin E and heart disease: a case study. Am. J. Clin. Nutr. 69 (suppl) (1999), S1322-S1329

[35] Law, M. R., Morris, J. K.: By how much does fruit and vegetable consumption reduce the risk of ischaemic heart disease? Eur. J. Clin. Nutr. 52 (1998), 549-556

[36] Levine, M., Rumsey, S. C., Daruwala, R., Park, J. B., Wang, Y.: Criteria and Recommendations for Vitamin C Intake. JAMA 281 (1999), 1415-1423

[37] Lewis, C. J., Yetley, E. A.: Health claims and observational human data: relation between dietary fat and cancer. Am. J. Clin. Nutr. 69 (suppl) (1999), S1357-S1364

[38] Malinow, M. R., Bostom, A. G., Krauss, R. M.: Homocyst(e)ine, diet, and cardiovascular diseases: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. Circulation 99 (1999), 178-182

[39] Omenn, G. S.: An assessment of the scientific basis for attempting to define the Dietary Reference Intake for beta carotene. J. Am. Diet. Assoc. 98 (1998), 1406-1409

[40] Omenn, G. S., Goodman, G. E., Thornquist, M. D. et al.: Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. N. Engl. J. Med. 334 (1996), 1150-1155

[41] Orimo, H., M. Shiraki, A. Tomita, H. Morii, T. Fujita, M. Ohata: Effects of menatetrenone on the bone and calcium metabolism in osteoporosis: A double-blind placebo-controlled study. J. Bone Miner. Metab. 16 (1998), 106-112

[42] Palan, P. R., Mikhail, M. S., Goldberg, G. L., Basu, J., Runowicz, C. D., Romney, S. L.: Plasma levels of ß-carotene, lycopene, canthaxanthin, retinol, and α- and γ-tocopherol in cervical intraepithelial neoplasia and cancer. Clin. Cancer Res. 2 (1996), 181-185

[43] Pandey, D. K., Shekelle, R., Selwyn, B. J., Tagney, C., Stamler, J.: Dietary vitamin C and β-carotene and risk of death in middle-aged men. The Western Electric Study. Am. J. Epidemiol. 142 (1995), 1269-1278

[44] Rapola, J. M., Virtamo, J., Haukka, J. K., Heinonen, O. P., Albanes, D., Taylor, P. R., Huttunen, J. K.: Effect of vitamin E and beta carotene on the incidence of angina pectoris. A randomized, double-blind, controlled trial. JAMA 275 (1996), 693-698

[45] Rapola, J. M., Virtamo, J., Ripatti, S., Huttunen, J. K., Albanes, D., Taylor, P. R., Heinonen, O. P.: Randomised trial of α-tocopherol and ß-carotene supplements on incidence of major coronary events in men with previous myocardial infarction. Lancet 349 (1997), 1715-1720

[46] Rapola, J. M.: Should we prescribe antioxidants to patients with coronary heart disease? Eur. Heart J. 19 (1998), 530-532

[47] Rimm, E. B., Ascherio, A., Giovannucci, E., Spiegelman, D., Stampfer, M. J., Willett, W. C.: Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. JAMA 275 (1996), 447-451

[48] Rimm, E. B., Stampfer, M. J., Ascherio, A., Giovannucci, E., Colditz, G. A., Willett, W. C.: Vitamin E consumption and the risk of coronary heart disease in men. N. Engl. J. Med. 328 (1993), 1450-1456

[49] Schneider, R., Eberhard, W., Heseker, H., Kübler, W.: Vitamin Intake and Vitamin Status in Germany. In: Walther, P.: The Scientific Basis for Vitamin Intake in Human Nutrition. Bibliotheca Nutritio et Dieta, No. 52, Karger, Basel (1995), 116-127

[50] Sempos, C.T., Liu, K., Ernst, N.D.: Food and nutrient exposures: what to consider when evaluating epidemiologic evidence. Am. J. Clin. Nutr. 96 (suppl) (1999), S1330-S1338

[51] Slattery, M. L., Berry, T. D., Potter, J., Caan, B.: Diet diversity, diet composition, and risk of colon cancer (United States). Cancer Causes Control 8 (1997), 872-882

[52] Stampfer, M. J., Hennekens, C. H., Manson, J. E., Colditz, G. A., Rosner, B., Willett, W. C.: Vitamin E consumption and the risk of coronary disease in women. N. Engl. J. Med. 328 (1993), 1444-1449

[53] Stampfer, M. J., Rimm, E. B.: Epidemiologic evidence for vitamin E in prevention of cardiovascular disease. Am. J. Clin. Nutr. 62 (1995), 1365S-1369S

[54] Statistisches Bundesamt (ed.): Gesundheitsbericht für Deutschland. Metzler-Poeschel, Stuttgart (1998)

[55] Stephens, N. G., Parsons, A., Schofield, P. M., Kelly, F., Cheeseman, K., Mitchinson, M. J.: Randomized controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study. Lancet 347 (1996), 781-786

[56] The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group: The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N. Engl. J. Med. 330 (1994), 1029-1035

[57] Watzl, B., Leitzmann, C.: Bioaktive Substanzen in Lebensmitteln. Hippokrates Verlag, Stuttgart, 2. Auflage (1999)

[58] World Cancer Research Fund/American Institute for Cancer Research: Food, Nutrition, and the Prevention of Cancer: a Global Perspective (1997), 424

[59] World Cancer Research Fund/American Institute for Cancer Research: Food, Nutrition, and the Prevention of Cancer: a Global Perspective (1997), 512

Section III: Appendix

Tables

Table I: Recommendations, estimated values, guiding values

Recommendations[1]	**Estimated values**[2]	**Guiding values**[3]
Protein	ß-Carotene[4]	Energy
Essential fatty acids	Vitamin E	Fat
Vitamin A	Vitamin K	Cholesterol
Vitamin D	Pantothenic acid	Carbohydrates
Thiamin	Biotin	Dietary fibre
Riboflavin	Sodium[4]	Alcohol
Niacin	Chloride[4]	Water
Vitamin B_6	Potassium[4]	Fluoride
Folate / folic acid	Selenium	
Vitamin B_{12}	Copper	
Vitamin C	Manganese	
Calcium	Chromium	
Phosphorus	Molybdenum	
Magnesium		
Iron		
Iodine		
Zinc		

[1] Recommended nutrient intake see table II

[2] See table III (except for ß-carotene, sodium, chloride, potassium)

[3] Not in table II or III; see tables and text in the corresponding chapters

[4] Not in table III (data referring to ß-carotene, sodium, chloride, potassium are provided in the text)

*Table II: Recommended nutrient intake per day **

Age	Protein g/kg[1]/day		Protein g/day		Essential fatty acids % of energy		Vitamin A mg RE[7]		Vitamin D[9] µg	Thiamin mg		Riboflavin mg		Niacin mg NE[12]	
	m	f	m	f	n-6	n-3[6]	m	f		m	f	m	f	m	f
Infants															
0 to under 4 months	2.7 / 2.0 / 1.5[2]		12 / 10 / 10[2]		4.0	0.5	0.5[6]		10[10]	0.2[6]		0.3[6]		2[6]	
4 to under 12 months	1.3 / 1.1[3]		10 / 10[3]		3.5	0.5	0.6		10[10]	0.4		0.4		5	
Children															
1 to under 4 years	1.0		14	13	3.0	0.5	0.6		5	0.6		0.7		7	
4 to under 7 years	0.9		15	17	2.5	0.5	0.7		5	0.8		0.9		10	
7 to under 10 years	0.9		24	24	2.5	0.5	0.8		5	1.0		1.1		12	
10 to under 13 years	0.9		34	35	2.5	0.5	0.9	0.9	5	1.2	1.0	1.4	1.2	15	13
13 to under 15 years	0.9		46	45	2.5	0.5	1.1	1.0	5	1.4[11]	1.1[11]	1.6[11]	1.3[11]	18[11]	15[11]
Adolescents and adults															
15 to under 19 years	0.9	0.8	60	46	2.5	0.5	1.1	0.9	5	1.3	1.0	1.5	1.2	17	13
19 to under 25 years	0.8		59	48	2.5	0.5	1.0	0.8	5	1.3	1.0	1.5	1.2	17	13
25 to under 51 years	0.8		59	47	2.5	0.5	1.0	0.8	5	1.2	1.0	1.4	1.2	16	13
51 to under 65 years	0.8		58	46	2.5	0.5	1.0	0.8	5	1.1	1.0	1.3	1.2	15	13
65 years and older	0.8		54	44	2.5	0.5	1.0	0.8	10	1.0	1.0	1.2	1.2	13	13
Pregnant women				58[4]	2.5	0.5		1.1[4]	5		1.2[4]		1.5[4]		15[4]
Lactating women				63[5]	2.5	0.5		1.5[8]	5		1.4		1.6		17

* Guiding values for intake of energy, fat, cholesterol, carbohydrates, dietary fibre, alcohol, water and fluoride and data about β-carotene, sodium, chloride and potassium are to be found in the corresponding chapters

1 Related to reference weight

2 0-1 / 1-2 / 2-4 months; see also text in the chapter 'Protein'

3 4-6 / 6-12 months; see also text in the chapter 'Protein'

4 From the 4th month of pregnancy

5 About 2 g of additional protein per 100 g of secreted milk

6 Estimated value

7 1 mg of retinol equivalent = 1 mg of retinol = 6 mg of all-trans-β-carotene = 12 mg of other provitamin A-carotenoids = 1.15 mg of all-trans retinyl acetate = 1.83 mg of all-trans retinyl palmitate; 1 IE = 0.3 µg retinol

8 About 70 µg of additional retinol equivalents per 100 g of secreted milk

9 1 µg = 40 IU; 1 IU = 0.025 µg

10 The German Paediatric Society *(Deutsche Gesellschaft für Kinderheilkunde)* recommends for prophylaxis of rickets in breast-fed and non-breast-fed infants a vitamin D tablet of 10-12.5 µg (400-500 IU) daily, starting upon completion of the 1st week of life throughout the 1st year of life, independent of vitamin D production by UV light in the skin and vitamin D intake with human milk or infant formulae (basic vitamination). Prophylaxis may be continued in the winter months of the 2nd year of live

11 The large value results from the relation to energy supply (table 4, page 26)

12 1 mg niacin equivalent = 60 mg of tryptophan

Vitamin B_6 mg		Folate µg FE[13]	Vitamin B_{12} µg	Vitamin C mg	Calcium mg	Phosphorus mg	Magnesium mg		Iron mg		Iodine µg		Zinc mg	
m	f						m	f	m	f[24]	D[28], WHO, A	CH	m	f
0.1[6]		60[6]	0.4[6]	50[6]	220[6]	120[6]	24[6]		0.5[6, 25, 26]		40[6]	50	1.0[6]	
0.3		80	0.8	55	400[6]	300	60		8[25]		80	50	2.0	
0.4		200	1.0	60	600	500	80		8		100	90	3.0	
0.5		300	1.5	70	700	600	120		8		120	90	5.0	
0.7		300	1.8	80	900	800	170		10		140	120	7.0	
1.0		400	2.0	90	1100	1250	230	250	12	15	180	120	9.0	7.0
1.4		400	3.0	100	1200	1250	310	310	12	15	200	150	9.5	7.0
1.6	1.2	400[14]	3.0	100[17]	1200	1250	400	350	12	15	200	150	10.0	7.0
1.5	1.2	400[14]	3.0	100[17]	1000	700	400	310	10	15	200	150	10.0	7.0
1.5	1.2	400[14]	3.0	100[17]	1000	700	350	300	10	15	200	150	10.0	7.0
1.5	1.2	400	3.0	100[17]	1000	700	350	300	10	10	180	150	10.0	7.0
1.4	1.2	400	3.0	100[17]	1000	700	350	300	10	10	180	150	10.0	7.0
	1.9[4]	600[14]	3.5[15]	110	1000[19]	800[21]		310[23]		30	230	200		10.0[4]
	1.9	600	4.0[16]	150[18]	1000[20]	900[22]		390		20[27]	260	200		11.0

[13] Calculation based on the total of folate-active compounds in the usual diet = folate equivalents (acc. to the new definition)
[14] Women planning a pregnancy or capable of becoming pregnant should ingest a supplementary 400 µg of synthetic folic acid (= pteroyl-monoglutamic acid/PGA) to prevent neural tube defects in the infant. Supplementary folic acid intake should begin not later than 4 weeks before pregnancy and be continued throughout the first trimester.
[15] Especially to maintain nutrient density
[16] About 0.13 µg of additional vitamin B_{12} per 100 g of secreted milk
[17] Smokers 150 mg/day
[18] Taking vitamin C secreted with 750 ml of breast milk into account
[19] Pregnant women under 19 years 1200 mg
[20] Lactating women under 19 years 1200 mg
[21] Pregnant women under 19 years 1250 mg
[22] Lactating women under 19 years 1250 mg
[23] Pregnant women under 19 years 350 mg
[24] Non-menstruating women who are neither pregnant nor breast-feeding a child: 10 mg/day
[25] Except for premature infants
[26] Dietary iron is not required before the 4th month due to the newborn's reserve of placental iron (Hb iron)
[27] This applies to breast-feeding and non-breast-feeding women for replacement of iron losses during pregnancy
[28] D = Germany, A = Austria, CH = Switzerland, WHO = World Health Organization

Table III: Estimated values for adequate intake per day

Age	Vitamin E mg TE[1, 2]		Vitamin K µg		Pantothenic acid mg	Biotin µg	Selenium µg	Copper mg	Manganese mg	Chromium µg	Molybdenum µg
	m	f	m	f							
Infants											
0 to under 4 months	3		4		2	5	5-15	0.2-0.6	—[4]	1- 10	7
4 to under 12 months	4		10		3	5-10	7-30	0.6-0.7	0.6-1.0	20- 40	20- 40
Children											
1 to under 4 years	6	5	15		4	10-15	10-40	0.5-1.0	1.0-1.5	20- 60	25- 50
4 to under 7 years	8	8	20		4	10-15	15-45	0.5-1.0	1.5-2.0	20- 80	30- 75
7 to under 10 years	10	9	30		5	15-20	20-50	1.0-1.5	2.0-3.0	20-100	40- 80
10 to under 13 years	13	11	40		5	20-30	25-60	1.0-1.5	2.0-5.0	20-100	50-100
13 to under 15 years	14	12	50		6	25-35	25-60	1.0-1.5	2.0-5.0	20-100	50-100
Adolescents and adults											
15 to under 19 years	15	12	70	60	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100
19 to under 25 years	15	12	70	60	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100
25 to under 51 years	14	12	70	60	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100
51 to under 65 years	13	12	80	65	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100
65 years and older	12	11	80	65	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100
Pregnant women		13		60	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100
Lactating women		17[3]		60	6	30-60	30-70	1.0-1.5	2.0-5.0	30-100	50-100

[1] 1 mg of RRR α-tocopherol equivalent = 1 mg of RRR α-tocopherol = 1.49 IU; 1 IU = 0.67 mg of RRR α-tocopherol = 1 mg of all-rac-α-tocopheryl acetate

[2] 1 mg of RRR α-tocopherol (D-α-tocopherol) equivalent = 1.1 mg of RRR α-tocopheryl acetate (D-α-tocopheryl acetate) = 2 mg of RRR β-tocopherol (D-β-tocopherol) = 4 mg of RRR γ-tocopherol (D-γ-tocopherol) = 100 mg of RRR δ-tocopherol (D-δ-tocopherol) = 3.3 mg of RRR α-tocotrienol (D-α-tocotrienol) = 1.49 mg of all-rac-α-tocopheryl acetate (D, L-α-tocopheryl acetate)

[3] Allowance of about 260 µg of RRR α-tocopherol equivalents per 100 g of secreted milk

[4] No data available; see text

Table IV: Energy and nutrient content in breast milk and infant formulae

Nutrient	**Breast milk**[1,2]		**Infant formulae**[3,4]
	Average (per 100 g)	Variability (per 100 g)	(per 100 g)
Energy (kJ)	288	—	250-315
Energy(kcal)	69	—	60-75
Protein (g)	1.13	1.03-1.43	1.3-2.1[5]
Fat (g)	4.03	3.50-4.62	3.1-4.6
Linoleic acid (g)	0.41	0.29-0.61	0.21-0.84
Carbohydrates (g)	7	—	5-10
Vitamin A (µg)[6]	69	53-74	42-126
Carotenoids (µg)	3.0	—	—
Vitamin D (µg)	0.07	0.01-0.12	0.7-1.75
Vitamin E (mg)[7]	0.28	0.15-0.54	≥ 0.5/g of polyunsaturated fatty acids
Vitamin K (µg)	0.48	0.3-4.0	≥ 2.80
Thiamin (µg)	15	13-17	≥ 28
Riboflavin (µg)	38	30-44	≥ 42
Niacin (mg)	0.17	0.13-0.20	≥ 0.56
Vitamin B_6 (µg)	14	9-17	≥ 25
Folate*/folic acid+(µg)	8.0*	3.7-8.5*	≥ 2.8+
Pantothenic acid (mg)	0.21	0.16-0.26	≥ 0.21
Biotin (µg)	0.58	0.40-1.00	≥ 1.05
Vitamin B_{12} (ng)	50	30-100	≥ 70
Vitamin C (mg)	6.5	3.5-7.8	≥ 5.6
Sodium (mg)	13	12-19	14-42
Chloride (mg)	40	32-49	35-88
Potassium (mg)	47	46-64	42-102
Calcium (mg)	29	22-41	≥ 35
Phosphorus (mg)	15	12-17	18-63
Magnesium (mg)	3.2	2.9-5.0	3.5-10.5
Iron (µg)	58	26-58	350-1050[8]
Iodine (µg)	5.1	0.5-9.0	≥ 3.5
Fluoride (µg)	17	13-25	—
Zinc (µg)	134	74-390	350-1050
Selenium (µg)	3.3	1.0-5.3	≤ 2.1[8]
Copper (µg)	35	22-77	14-56
Manganese (µg)	0.71	0.70-1.40	—
Chromium (µg)	4.1	3.0-80	—
Molybdenum (µg)	1.0	—	—

1 Souci, S. W., Fachmann, W., Kraut, H.: Die Zusammensetzung der Lebensmittel. Nährwert-Tabellen. 6. Auflage, medpharm Scientific Publishers, Stuttgart (2000)
2 Mature breast milk (≥ 10 days post partum)
3 Extracts from the EC regulations governing infant formulae and follow-on formulae 91/321/EWG; 96/4/EC)
4 Calculated from original data (data per 100 kcal were converted)
5 Cow's milk proteins
6 Retinol equivalents
7 Tocopherol equivalents
8 For products to which the respective nutrient has been added
— Data not available

Working Group 'Reference values for nutrient intake'

Elmadfa, Ibrahim Univ.-Prof. Dr.	Institut für Ernährungswissenschaften der Universität Wien
Erbersdobler, Helmut Prof. Dr.	Institut für Humanernährung und Lebensmittelkunde Christian-Albrechts-Universität Kiel
Gaßmann, Berthold Prof. Dr.	Deutsches Institut für Ernährungsforschung Bergholz-Rehbrücke
Stehle, Peter Prof. Dr.	Institut für Ernährungswissenschaften Rheinische Friedrich-Wilhelms-Universität Bonn
Walter, Paul Prof. Dr.	Biochemisches Institut der Universität Basel
Wolfram, Günther Prof. Dr. (Coordinator)	Institut für Ernährungswissenschaft Technische Universität München Freising-Weihenstephan

Scientific Secretary

Leschik-Bonnet, Eva; Dr.	Deutsche Gesellschaft für Ernährung e.V. Bonn

Contributors to the 'Reference values for nutrient intake'

Anke, M.; Prof. Dr.	Institut für Ernährung und Umwelt Friedrich-Schiller-Universität Jena
Amado, R.; Prof. Dr.	Institut für Lebensmittelwissenschaft ETH Zentrum Zürich / Schweiz
Barth, Chr.; Prof. Dr.	Deutsches Institut für Ernährungsforschung Bergholz-Rehbrücke
Baumgartner, Regula; Dr.	Universitäts-Kinderspital Basel
Bergmann, K. E.; Prof. Dr.	Robert Koch-Institut Berlin
Bergmann, Renate L; Prof. Dr.	Geburtsmedizinische Klinik (Department of Obstetrics) Charité-Virchow-Klinikum der Humboldt-Universität Berlin
Biesalski, H. K.; Prof. Dr.	Institut für Biologische Chemie und Ernährungswissenschaft Universität Stuttgart-Hohenheim Stuttgart
Bitsch, R.; Prof. Dr.	Institut für Ernährung und Umwelt Friedrich-Schiller-Universität Jena
Elmadfa, I.; Univ.-Prof. Dr.	Institut für Ernährungswissenschaften der Universität Wien
Gaßmann, B.; Prof. Dr.	Deutsches Institut für Ernährungsforschung Bergholz-Rehbrücke

Großklaus, R.; Prof. Dr.	Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin Berlin
Hauner, H.; Prof. Dr.	Diabetes-Forschungsinstitut Düsseldorf
Heseker, H.; Prof. Dr.	Universität-Gesamthochschule Paderborn
Hurrell, R.; Prof. Dr.	Swiss Federal Institute of Technology Lab. for Human Nutrition Rüschlikon
Jahreis, G.; Prof. Dr.	Institut für Ernährung und Umwelt Friedrich-Schiller-Universität Jena
Kasper, H.; Prof. Dr.	Medizinische Klinik der Universität Würzburg
Keller, U.; Prof. Dr.	Dep. Innere Medizin - Abt. für Endokrinologie und Diabetologie und klinische Ernährung Kantonsspital Basel
Kersting, Mathilde; PD Dr.	Forschungsinstitut für Kinderernährung Dortmund
Köhrle, J.; Prof. Dr.	Medizinische Poliklinik der Universität Abt. für Molekulare Innere Medizin Würzburg
König, J. S.; Dr.	Institut für Ernährungswissenschaften der Universität Wien
Koletzko, B.; Prof. Dr.	Kinderklinik im Dr. von Haunerschen Kinderspital Klinikum Innenstadt Ludwig-Maximilians-Universität München

Kries, R. von; Prof. Dr.	Institut für Soziale Pädiatrie und Jugendmedizin Ludwig-Maximilians-Universität München
Lombeck, Ingrid; Prof. Dr.	Zentrum für Kinderheilkunde Heinrich-Heine-Universität Düsseldorf
Manz, F.; Prof. Dr.	Forschungsinstitut für Kinderernährung Dortmund
Metges, Cornelia; Dr.	Deutsches Institut für Ernährungsforschung Bergholz-Rehbrücke
Müller, M. J.; Prof. Dr.	Institut für Humanernährung und Lebensmittelkunde Christian-Albrechts-Universität Kiel
Neuhäuser-Berthold, Monika; Prof. Dr.	Institut für Ernährungswissenschaft Justus-Liebig-Universität Giessen
Noack, R.; Prof. Dr.	Deutsches Institut für Ernährungsforschung Bergholz-Rehbrücke
Pfannhauser, W.; Univ.-Prof. Dr.	Institut für Biochemie Technische Universität Graz Graz
Pickardt, Caroline-Renate; Prof. Dr.	Medizinische Klinik - Klinikum Innenstadt Ludwig-Maximilians-Universität München
Pietrzik, K.; Prof. Dr.	Institut für Ernährungswissenschaft Rheinische Friedrich-Wilhelms-Universität Bonn
Rechkemmer, G.; Prof. Dr.	Institut für Ernährungsphysiologie Bundesforschungsanstalt für Ernährung Karlsruhe

Schümann, K.; PD Dr.	Walter Straub-Institut für Pharmakologie und Toxikologie Ludwig-Maximilians-Universität München
Schutz, Y.; Prof. Dr.	Institute de Physiologie Université de Lausanne Lausanne
Schweigert, F. J.; Prof. Dr.	Institut für Ernährungswissenschaft Universität Potsdam Bergholz-Rehbrücke
Scriba, P.; Prof. Dr.	Medizinische Klinik - Klinikum Innenstadt Ludwig-Maximilians-Universität München
Sievers, Erika; PD Dr.	Kinderklinik Christian-Albrechts-Universität Kiel
Volkert, Dorothee; PD Dr.	Institut für Ernährungswissenschaft Rheinische Friedrich-Wilhelms-Universität Bonn
Watzl, B.; Dr.	Institut für Ernährungsphysiologie Bundesforschungsanstalt für Ernährung Karlsruhe
Wenk, C.; Prof. Dr.	Institut für Nutztierwissenschaft / Gruppe Ernährung ETH-Zentrum Zürich
Wolfram, G.; Prof. Dr.	Institut für Ernährungswissenschaften Technische Universität München Freising-Weihenstephan
Zittermann, A.; PD Dr.	Institut für Ernährungswissenschaft Rheinische Friedrich-Wilhelms-Universität Bonn

Abbreviations

m = male
f = female
BW = Body Weight
IU = International Units
kJ = Kilojoule
MJ = Megajoule
kcal = Kilocalories
kg = Kilogram
mg = Milligram
µg = Microgram
l = Litre
ml = Millilitre
µmol = Micromol
mosm = Milliosmol

DGE = German Nutrition Society
DRI = Dietary Reference Intakes
ÖGE = Austrian Nutrition Society
PAL = Physical Activity Level
RDA = Recommended Dietary Allowances
SGE = Swiss Society for Nutrition Research
SVE = Swiss Nutrition Association
VERA = Cooperative study: Nutrition Survey and Risk Factor Analysis